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THE CLINICAL VALUE OF RENAL BIOPSY.[1]

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THE exact diagnosis of renal disease has always been rather uncertain during life, and sometimes equally uncertain at autopsy. Correlation of the clinical features and the morbid anatomy of kidney disease was slow in historical evolution and has remained inexact and unsatisfactory to this date.

Rhuphos of Ephesus, who lived about A.D. 100, first described the association of sclerosis of the kidneys with dropsy (Major, 1954). In 1811, William Charles Wells noted the presence of albuminuria in some cases of dropsy, and commented on the gross appearance of the kidneys in these cases. However, it was left to Richard Bright in 1827 to define clearly the range of diseases which since then have borne his name. He stressed that the reports of his medical cases were "selected with a view of illustrating the symptoms and cure of disease by reference to morbid anatomy". Jacob Henle in 1847 carried out careful microscopic studies of the kidneys in health and in disease, and since that time few major basic advances have occurred in the clinico-pathological correlation of chronic renal disease.

Biopsy of the kidney may be expected to provide an ætiological diagnosis during life, if the tissue removed is representative and the histological changes are of such a nature as to be clearly categorized. Such a procedure can be justified only if it is easy to perform and carries a negligible morbidity and mortality. The procedure should benefit the patient, not merely satisfy the clinician's curiosity.

How far renal biopsy fulfils these criteria remains unanswered at present, although over one thousand renal biopsies have been done (Iversen and Brun, 1951; Alwall, 1952; Kark and Muehrcke, 1954; Taft *et alii*, 1954; Brun, 1954; Jackson *et alii*, 1955; Kunis *et alii*, 1955; Parrish and Howe, 1955; Ross and Ross, 1957), and we have performed needle biopsy of the kidney in 51 cases to assess its clinical value in the diagnosis and prognosis of renal disease.

Technique.

The technique used is that described by Kark and Muehrcke (1954), except that a Franseen biopsy needle with a sharp, serrated, cutting edge was used instead of the modified Vim-Silverman needle.

Pre-biopsy studies included a plain X-ray examination of the abdomen in inspiration and expiration, or else

[1] Read at a meeting of The Royal Australasian College of Physicians, June 6, 1958.

an intravenous pyelographic examination in the prone position, microscopic examination and culture of the urine, blood hæmoglobin estimation and determination of blood urea content and prothrombin index. Patients were excluded who had a solitary kidney, rapidly progressing azotæmia, renal neoplasm, hydronephrosis or a bleeding tendency. Premedication consisted of pentobarbitone, three grains every two hours, pethidine, 50 milligrammes given intramuscularly, and "Largactil", 50 milligrammes half an hour before biopsy.

Biopsy was performed in the ward with the patient in the prone position, and a cylindrical sandbag was placed under the upper part of the abdomen. The sandbag tends to splint the kidney and to aid hæmostasis after the biopsy. However, it is uncomfortable to the subject, and seemed to be a factor in pre-biopsy restlessness and emesis. It also limits the longitudinal excursion of the kidney during respiration, so that accurate localization of the kidney may not be possible. The right kidney is usually selected for biopsy through fear of bleeding resulting from splenic puncture on the left side. This would not appear to be a great hazard if the kidney is accurately localized. In this series, biopsy of the left kidney was successfully performed on four occasions without complication. "Xylocaine" (2%) was used as a local anæsthetic.

A fine, exploring, lumbar puncture needle is introduced through the back, below the twelfth rib, at a site determined by the skiagrams to be over the lower lateral pole of the kidney. The kidney has been penetrated when the operator feels the needle penetrate the lumbar fascia resistance, the perinephric void and the renal capsule resistance and when the exploring needle swings through a wide arc on respiration. However, there may be little tactile information when the kidney is soft and œdematous, as in the nephrotic syndrome. A valuable sign in these cases has been a gentle rocking movement of the needle synchronous with the pulse. The exploring needle may not swing with expected vigour during respiration. This may be due to lack of mobility of the kidney itself, to excessive splinting by the sandbag or purely to costal breathing. Removal of the sandbag and instruction in correct diaphragmatic respiration usually corrected these difficulties. When the biopsy needle is considered to be in the kidney substance, the patient is instructed to cease breathing. The stilette is withdrawn. A ten-millilitre Luer-Lok syringe is connected to the needle and suction applied. To obtain the core of renal tissue the needle is advanced through the kidney while suction is maintained. The tissue is immediately transferred to a 5% formalin solution.

Biopsy was successful on 53 occasions in 51 cases after 59 attempts. The core measured two millimetres by five to 20 millimetres. Renal tissue was obtained from the cortex and medulla in 52 cases; in one case medulla only was extracted. The maximum number of glomeruli contained in a specimen was 42; the average count was 16.

Complications.

Muehrcke (1956) has remarked that "although renal biopsy is a most valuable, practical, clinical tool, it is not an office procedure". Backache, renal colic, hæmaturia and retroperitoneal hæmorrhage have been reported as complications (Alwall, 1952; Muehrcke *et alii*, 1955; Ross and Ross, 1957). In about 1000 cases reported, there have been two deaths due to the procedure (Alwall, 1952; Zelman, 1954).

In our series, after 59 attempted renal biopsies, six patients suffered complications. There were no deaths. Macroscopic hæmaturia occurred in all six patients and persisted for longer than 24 hours in three of them. The following patient required transfusion and subsequent surgical intervention.

A man, aged 48 years, had established renal failure from suspected chronic pyelonephritis. His blood urea content was 105 milligrammes per 100 millilitres. Renal biopsy was performed without technical difficulty, but it was noted during biopsy that the kidney consistency was hard. Histologically, the tissue revealed advanced chronic pyelonephritis with superadded changes of nephrosclerosis. After biopsy the patient began to show intermittent macroscopic hæmaturia. Blood transfusion was deemed necessary at the end of two weeks. His deteriorating clinical condition and the persistent nature of the hæmorrhages made nephrectomy necessary. Examination of the kidney after operation showed necrotizing papillitis associated with pyelonephritis. The origin of the hæmaturia appeared to be a necrotic renal pyramid. The temporal relationship suggested that the biopsy procedure may have initiated or aggravated changes that subsequently led to the development of necrotizing papillitis. After operation the patient improved, and twelve months later was alive and had a blood urea content of 32 milligrammes per 100 millilitres.

In two patients biopsy was followed by aggravation of a pre-existing infection, in addition to the hæmaturia.

A woman, aged 37 years, was admitted to hospital with renal insufficiency and chronic infection of the urinary tract with *Bacillus proteus*. Biopsy was performed at a time when she was febrile and when the positive result of blood culture for *Staphylococcus pyogenes* was not at hand. The biopsy specimen showed chronic pyelonephritis, but failed to grow organisms on attempts at culture.

A man, aged 38 years, was admitted to hospital with an acute flare-up of chronic bronchiectasis. Biopsy was performed because of hypertension, œdema and proteinuria of uncertain origin. The patient was febrile at the time of biopsy and specimens of his sputum yielded a profuse growth of *Staph. pyogenes*. Histological examination of specimens of the kidney revealed acute glomerulonephritis.

Attempts at post-biopsy blood cultures in both these cases produced no growths, but in each an infective process seemed to have been aggravated by the procedure. The exact mechanism of aggravation was obscure.

These complications occurred in the early part of the series, and suggested that case selection had not been sufficiently stringent. It is in the group of acute infection, active pyelonephritis and uncontrolled hypertension that the complications have occurred. By way of contrast, in 21 cases with the nephrotic syndrome, no untoward sequelæ resulted from the biopsy. The procedure itself occasions the patient very little discomfort and is well tolerated.

We believe that in the presence of acute infection, renal or extrarenal, biopsy should be deferred. Hypertension should be controlled by medical methods whenever possible before biopsy is attempted. The presence of advanced renal failure adds to the hazard of biopsy, and would make any information gained by this procedure unlikely to be of benefit to the patient.

Indications for Biopsy.

As yet no absolute indications for the use of renal biopsy have been established. In general, we have been interested in establishing the ætiology and severity in cases of the nephrotic syndrome and the ætiology in cases of hypertension, particularly in young people. We had hoped that the procedure would be of value in the diagnosis and isolation of the organism in difficult cases of pyelonephritis, but in such cases results have been disappointing. We have been willing to perform a biopsy in cases of renal disease, the nature of which was clinically uncertain. We have thought that the younger the patient, the less advanced the disease process, and the more uncertain the clinical diagnosis, the more biopsy was indicated.

Correlation of Clinical and Histological Diagnosis.

The clinical diagnosis was confirmed in 22 of 51 cases. In another 10 cases, all of the nephrotic syndrome, the biopsy specimen contained no recognizable abnormality. In eight of these the clinical diagnosis was the nephrotic stage of chronic glomerulonephritis, and in the other two, bilateral renal vein thrombosis. The normal appearances in some renal biopsy specimens in these conditions will be discussed later. In 13 cases the provisional diagnosis was altered after renal biopsy. Three other cases were suspected histologically to be examples of lupus nephritis. In none of these were L.E. cells demonstrated in the peripheral blood, but the clinical picture in retrospect was compatible with such a diagnosis. In three further cases, the tissue removed by biopsy was not representative.

If normal findings on renal biopsy are accepted as being compatible with the nephrotic stage of glomerulonephritis, it may be claimed that in 32 cases the histological diagnosis correlated well with the clinical impression, confirmed the clinical diagnosis and gave an estimate of the severity of the lesion. In 13 cases the findings on renal biopsy altered the clinical diagnosis, and in some of these cases changes in therapy and prognosis resulted. In six cases the results of biopsy were indefinite.

Nephrotic Syndrome.

In 21 cases of the nephrotic syndrome the ages of the patients varied from 14 to 67 years, more than half being younger than 35 years. The duration of illness varied from two months to seven years. All patients were examined by biopsy whilst still œdematous, and all manifested proteinuria, hypoproteinæmia and hypercholesterolæmia.

Table I shows that chronic membranous glomerulonephritis (Allen, 1951) was diagnosed histologically in seven cases. In eight others, identical clinically, the appearance on biopsy was normal. It seems probable that the finding of normal renal tissue in these cases represents an early and potentially reversible stage in the development of chronic membranous glomerulonephritis.

TABLE I.

Correlation of Clinical and Histological Diagnosis in 21 Cases of the Nephrotic Syndrome.

Provisional Diagnosis.	Histological Diagnosis.	Number of Cases.
Nephrotic phase of chronic glomerulonephritis.	Normal tissue	8
	Chronic membranous glomerulonephritis ..	7
Acute progressive glomerulonephritis (less than three months after acute episode).	Normal tissue	2
	Diffuse subacute glomerulonephritis	2
Renal vein thrombosis.	Normal tissue	2

In two cases the picture was that of a diffuse subacute glomerulonephritis (Allen, 1951). Clinically, these cases appeared to have progressed within three months into a nephrotic state after an attack of acute glomerulonephritis. Two further patients with similar histories suggesting progression to the nephrotic stage after an attack of acute nephritis showed normal renal tissue. Both subsequently responded well to medical treatment and seemed to follow a similar course to the other group of nephrotic patients with a normal appearance on biopsy. The demonstration of normal renal tissue by biopsy in two cases of patients suspected of suffering from bilateral renal vein thrombosis was not of definite diagnostic value. Subsequent events suggested that neither, in fact, suffered from that condition.

The relationship between the presence of visible glomerular abnormalities and the patient's response to steroid therapy and other medical agents was of interest. Fourteen patients with the nephrotic syndrome were given steroids, and seven of these responded, with a satisfactory diuresis and clinical improvement. Of the 14 patients, seven had visible glomerular abnormalities and seven had normal renal tissue. In the group with normal tissue, only one patient failed to have a diuresis when treated with steroids. Contrariwise, only one patient with histological glomerular abnormality achieved a diuresis while on steroid therapy; one might assume that the finding of normal tissue in patients with the nephrotic syndrome would be an indication for vigorous steroid therapy, and that a satisfactory outcome could be expected in most cases.

There appeared to be no correlation between the degree of glomerular damage, as determined by biopsy, and the magnitude of the proteinuria.

The relationship between the presence of hypertension and the demonstration of glomerular abnormality by biopsy was not clear. Hypertension occurred occasionally in the presence of a normal appearance on biopsy, but it was inconstant and sometimes seemed to follow treatment such as steroids or the intravenous administration of albumin. Hypertension was sustained in two patients with moderately advanced chronic membranous glomerulonephritis.

The following reports of cases show some aspects of the value of renal biopsy in the nephrotic syndrome.

CASE I.—A boy, aged 14 years, was believed to have had "nephritis" in 1952. He suffered recurrent sore throats, but otherwise was well until January, 1956, when gross œdema and ascites developed. He was admitted to hospital in October, 1956, when he was still œdematous and had a prostatic abscess. His blood pressure was recorded as 140/90 millimetres of mercury. His urine showed "heavy proteinuria" and occasional blood and pus cells. Laboratory investigations revealed a blood urea content of 16 milligrammes per 100 millilitres, a serum protein level of 1·8 grammes per 100 millilitres, and a serum cholesterol level of 620 milligrammes per 100 millilitres. Renal biopsy revealed what was considered to be normal tissue (Figure I) (glomerular count, 18). After a course of albumin given by intravenous infusion and of prednisone, he had prompt diuresis and was discharged from hospital free of œdema.

CASE II.—A woman, aged 20 years, was admitted to hospital with a well-documented history of the nephrotic syndrome for seven years. During that time relapses in her condition had been successfully treated by sodium restriction, mercurial diuretics, ion exchange resins and steroids. In October, 1957, she was again œdematous and had ascites. Her blood pressure was 130/80 millimetres of mercury. Urinary protein loss was 15 grammes in 24 hours. Microscopic examination of the urine showed moderate numbers of hyaline casts, but no pus. Attempt at culture produced no growth. Biochemical tests gave these findings: blood urea content 28 milligrammes per 100 millilitres, serum protein content 2·8 grammes per 100 millilitres, and serum cholesterol level 1000 milligrammes per 100 millilitres. No lupus erythematosus cells were detected in her peripheral blood. Renal biopsy disclosed chronic membranous glomerulonephritis (Figure II) and areas which could represent chronic pyelonephritis (glomerular count, 30). Diuresis was induced by a course of albumin given by intravenous infusion with lessening of œdema.

CASE III.—A man, aged 67 years, was admitted to hospital with the diagnosis of refractory congestive cardiac failure. He had been treated with digitalis and mercurial diuretics before his admission to hospital, with no relief in his clinical condition. On examination he had gross œdema of his legs, and ascites was demonstrated. The forearm venous pressure was normal (seven millimetres of saline). The daily urinary protein loss was 10 grammes. His blood pressure was 160/80 millimetres of mercury. An electrocardiogram showed digitalis effect, but otherwise showed no abnormalities. An X-ray examination of the chest showed slight cardiac enlargement. Biochemical analysis of the blood gave the following findings: blood urea content 135 milligrammes per 100 millilitres, serum protein level four grammes per 100 millilitres, and serum cholesterol level 800 milligrammes per 100 millilitres. The clinical diagnoses considered were bilateral renal vein thrombosis, glomerulonephritis and mercurial intoxication. Renal biopsy showed chronic membranous glomerulonephritis (glomerular count, 20). He showed no response to steroid therapy and died five weeks after biopsy. The biopsy diagnosis was confirmed at autopsy.

CASE IV.—A woman, aged 39 years, was considered to have had "toxæmia of pregnancy" with each of her pregnancies, in 1938, 1947, 1948 and 1953. In October, 1954, she developed a sore throat, after which œdema of the lower part of the limbs appeared. This episode was considered to be an attack of acute glomerulonephritis. She remained œdematous till her admission to hospital in April, 1956. Her blood pressure was 150/100 millimetres of mercury. The daily protein loss in the urine was nine grammes. The urinary sediment contained red blood cells and granular and hyaline casts. The blood urea content was 62 milligrammes per 100 millilitres, serum protein content 5·1 grammes per 100 millilitres, and serum cholesterol level 520 milligrammes per 100 millilitres. Renal biopsy disclosed chronic glomerulonephritis passing into the sclerotic stage (glomerular count, 4). She showed no response to a course of steroid therapy.

Hypertension.

The ætiology of hypertension, especially in the younger age group, is a matter of considerable importance in treatment and prognosis. It was believed that renal biopsy might have a contribution to make in the study of these patients, although focal lesions such as chronic pyelonephritis and early malignant hypertension may not always be demonstrated by biopsy when in fact they exist. We also expected to find some normal results to biopsies in early essential hypertension.

Sixteen patients with significant hypertension were subjected to renal biopsy (Table II). Normal tissue was obtained in six cases. These probably represented essential hypertension. It was of interest that the ages of the patients were 17, 19, 28, 29, 30 and 47 years. These were patients without a positive family history of hypertension, and the clinical diagnosis had been considered to be chronic glomerulonephritis.

TABLE II.

Correlation of Clinical and Histological Diagnosis in 16 Patients with Hypertension.

Provisional Diagnosis.	Histological Diagnosis.	Number of Cases.
Chronic pyelonephritis.	Chronic pyelonephritis.. ..	1
	Chronic glomerulonephritis ..	1
Chronic glomerulonephritis.	Chronic glomerulonephritis ..	5
	Normal tissue ..	4
Acute glomerulonephritis.	Acute glomerulonephritis ..	1
Diabetic glomerulosclerosis.	Diabetic glomerulosclerosis ..	2
Essential hypertension.	Normal tissue	2

Chronic pyelonephritis accounted for only one case of hypertension in this series, although it was diagnosed by biopsy in nine instances in the absence of hypertension. In five of the latter it had been overlooked clinically.

The following reports of cases are included to show some of these features.

CASE V.—A farmer, aged 26 years, complained of headache for six weeks and visual deterioration for two weeks. He had no past history of renal disease, but had a family history of hypertension. He had a blood pressure of 240/130 millimetres of mercury, papilœdema and retinal hæmorrhages with exudates. Examination of his urine showed it to contain "one-quarter" albumin, and it was normal microscopically. *Bacterium coli* was cultured from specimens of the urine. Biochemical findings were as follows: blood urea content 167 milligrammes per 100 millilitres, serum protein level 5·5 grammes per 100 millilitres, and serum cholesterol level 230 milligrammes per 100 millilitres. A blood count gave the following results: hæmoglobin value, 11·5 grammes per 100 millilitres; white cells numbered 4500 per cubic millimetre, with a normal cell distribution and type. Renal biopsy showed advanced chronic glomerulonephritis (Figure III) (glomerular count, 10). In spite of treatment, including "Ansolysen", he followed a fulminating downhill course, and died three months after symptoms commenced.

CASE VI.—A man, aged 19 years, was refused employment in a bank because of symptomless hypertension detected at the staff medical examination. He had no family history of hypertension or past history of renal disease. His blood pressure was 240/150 millimetres of mercury. There was no retinopathy. His urine was normal except for a trace of protein. Tests of renal function showed impaired ability to concentrate urine. The hæmoglobin value was 16·7 grammes per 100 millilitres; white cells numbered 11,900 per cubic millimetre; the blood urea content was 29 milligrammes per 100 millilitres; and the serum cholesterol level was 180 milligrammes per 100 millilitres. An intravenous pyelogram and a "Regitine" test showed no abnormality. Renal biopsy produced a glomerular count of 30. The tissue was considered to be within normal limits. He responded promptly and well to "Ansolysen" and "Serpasil".

CASE VII.—A woman, aged 29 years, was found in January, 1956, to have hypertension (blood pressure, 160/125 millimetres of mercury) when ten weeks pregnant. She had had severe bronchiectasis and cystic lungs for ten years and was dyspnœic. Her blood urea content was 34 milligrammes per 100 millilitres and her kidneys showed impaired concentrating ability. Pregnancy was terminated, and her renal lesion was believed to be chronic glomerulonephritis. In March, 1956, she developed ankle and facial œdema; her blood pressure was 160/120 millimetres of mercury, and examination of her urine showed it to contain "one-quarter" albumin. Her blood urea level was 31 milligrammes per 100 millilitres, serum protein level 6·7 grammes per 100 millilitres, serum cholesterol level 300 milligrammes per 100 millilitres. A carbon dioxide combining power of 38 milli-equivalents per litre was interpreted as reflecting respiratory acidosis. She showed no hypokalæmia or potassium-losing tendency. Although no hæmaturia was detected, it was considered that this episode was acute on chronic nephritis. Her œdema soon cleared spontaneously.

She was readmitted to hospital in August, 1956, for assessment of renal function. Her urinary findings were similar to those on the previous admission. Microscopic examination of the urine showed it to be normal, and there was minimal proteinuria; there was no retinopathy; the blood pressure was 160/120 millimetres of mercury, and the blood urea level was 30 milligrammes per 100 millilitres. Renal biopsy showed normal tissue and excluded amyloidosis and chronic glomerulonephritis as a diagnosis. Chronic pyelonephritis probably could not be excluded by biopsy, but at no stage did she manifest any clinical evidence of this condition.

Miscellaneous Renal Conditions.

Four further cases illustrate the role of renal biopsy in conditions of diagnostic difficulty.

CASE VIII.—A boy, aged 16 years, developed rheumatic fever in 1946. He had recurrent attacks until early 1957, when chronic rheumatic heart disease with mitral stenosis, incompetence and aortic valvular disease was diagnosed. In August, 1957, he developed gross œdema of his legs, arms and face, associated with heavy proteinuria. His blood pressure was 120/90 millimetres of mercury, his blood urea content 30 milligrammes per 100 millilitres. He was regarded as having "Type II nephritis" and was admitted to hospital for treatment. When examined he was cyanosed and œdematous, and apparently in heart failure. His cardiac murmurs were those of incompetence and stenosis of both mitral and aortic valves. He had minimal proteinuria; the blood urea level was 72 milligrammes per 100 millilitres and the serum bilirubin level 0·7 milligramme per 100 millilitres. He ran a low-grade fever. Blood cultures yielded negative results and a lupus erythematosus preparation was "negative". His urinary sediment contained an occasional red cell. One week after being in hospital he developed a right innominate vein thrombosis. The diagnosis was uncertain. Bilateral renal vein thrombosis, chronic glomerulonephritis and renal lesion of severe congestive cardiac failure were considered. Renal biopsy showed foci of fibrinoid necrosis in the glomeruli, changes possibly representing focal embolic glomerulonephritis (glomerular count, 27). Anticoagulants were suspended and he was watched carefully, with the diagnosis of subacute bacterial endocarditis in mind. Subsequent events confirmed that diagnosis. His clinical condition improved dramatically on the institution of the therapeutic regime for subacute bacterial endocarditis, and after four weeks no evidence of renal disease could be found.

CASE IX.—A young married woman, aged 27 years, had suffered since 1938 from diabetes mellitus which was treated with insulin. In 1951 she developed an attack of acute pyelonephritis. In 1954 she was admitted to hospital with the clinical diagnosis of Kimmelstiel-Wilson syndrome. She had œdema, proteinuria, hypertension (blood pressure 160/105 millimetres of mercury) and early diabetic retinopathy. The urinary sediment showed 20 to 30 leucocytes and five to eight red cells per high power field, and culture of the urine yielded a profuse growth of *B. coli*. The blood urea content was 34 milligrammes per 100 millilitres, serum cholesterol level 535 milligrammes per 100 millilitres. After one month she had lost her œdema and her retina appeared normal. However, her blood pressure remained high and proteinuria persisted.

By 1956 she was quite well, and because her blood pressure had returned to normal limits the original diagnosis was changed to that of a presumed attack of acute nephritis and pyelonephritis.

She was readmitted to hospital in 1956 for assessment of the renal status because she desired to have a family. She appeared normal except for minimal proteinuria. Renal biopsy disclosed moderately severe diffuse diabetic glomerulosclerosis (glomerular count, 22).

CASE X.—A young man, aged 19 years, was rejected for National Service because of symptomless proteinuria. He had no past history of nephritis, but proteinuria had been detected seven years previously at a school medical examination. He had no œdema, and his blood pressure was recorded as 120/70 millimetres of mercury. Heavy proteinuria was recorded. The results of biochemical tests were as follows: blood urea level 39 milligrammes per 100 millilitres, serum protein level 4·3 grammes per 100 millilitres, serum cholesterol level 390 milligrammes per 100 millilitres, hæmoglobin value 13·6 grammes per 100 millilitres. The urinary sediment contained granular casts and 2 to 10 red cells per high power field. The proteinuria was not orthostatic. An intravenous pyelogram showed no abnormality. Renal biopsy showed early chronic membranous glomerulonephritis (glomerular count, 15).

CASE XII.—A woman, aged 24 years, developed arthritis of her left ankle which lasted four days. After this, painful

red nodules appeared on her legs. These were diagnosed as erythema nodosum and lasted a few days. Two months later she had amenorrhœa, and during a prenatal examination proteinuria was detected. On her admission to hospital the pregnancy was not confirmed. Her urine deposit contained occasional pus and blood cells and culture yielded *B. coli*. The result of ward testing for proteinuria was recorded as "one-third". The hæmoglobin value was 12·0 grammes per 100 millilitres, leucocytes numbered 6400 per cubic millimetre, the sedimentation rate was raised, and the blood urea level was 24 milligrammes per 100 millilitres. She had pyrexia, which lasted three days, and after this hæmaturia became evident macroscopically; no lupus erythematosus cells were demonstrated in three tests; the Mantoux test (1:1000) gave no reaction. She was considered to have acute on chronic pyelonephritis, although sarcoidosis and tuberculosis were suspected. Renal biopsy showed fairly advanced chronic membranous glomerulonephritis, which because of its focal distribution in some glomeruli suggested lupus nephritis (Figure IV) (glomerular count, 27).

Discussion.

The value of renal biopsy in medicine could be academic or practical, or both. It could contribute to knowledge of the natural history and evolution of diseases affecting the kidneys and also be of use as a diagnostic and prognostic aid in a specific case in clinical practice.

Renal biopsy has been of definite value in the study of the early changes and histological progression in various renal diseases such as diabetic nephropathy (Brun *et alii*, 1953; Taft *et alii*, 1954), disseminated lupus erythematosus (Lister and Baker, 1954; Muehrcke *et alii*, 1957; Joske and Stubbe, 1957), renal calcinosis (Bjørneboe *et alii*, 1952), pyelonephritis (Jackson *et alii*, 1955; Kipnis *et alii*, 1955), anuria (Brun, 1954; Gormsen *et alii*, 1955), toxæmia of pregnancy (Pollak *et alii*, 1956), myelomatosis (Greenwald *et alii*, 1953) and the nephrotic syndrome (Bjørneboe *et alii*, 1952; Muehrcke *et alii*, 1954). These studies have added a greater understanding to our knowledge of diseases affecting the kidney. Correlative studies of histopathology and function have been reported in lupus nephritis (Muehrcke *et alii*, 1957) and in pyelonephritis (Kipnis *et alii*, 1955).

Correlative studies of clinical and histological diagnosis on the spectrum of renal diseases met with in a general medical unit are not as numerous as reports on individual disease processes. In 100 renal biopsies, Parrish and Howe (1955) found that renal biopsy proved the clinical impression incorrect in 52 and confirmed the clinical impression in 39, and in nine neither the pathologist nor the clinician could arrive at a definite diagnosis. Ross and Ross (1957), on the other hand, in 26 biopsies obtained only one unexpected diagnosis. Kark and Muehrcke (1954) stated that in 47 biopsies performed, the clinical diagnosis was changed in 25 and confirmed in 22.

In our series of 51 patients, the clinical diagnosis was confirmed histologically in 22 and was compatible in a further 10. In 13 the provisional diagnosis was altered as a result of biopsy, and in six cases the significance of the biopsy appearances was uncertain. The diseases which biopsy showed to be present most frequently when not thought likely clinically were either chronic pyelonephritis or chronic glomerulonephritis.

The tissue removed by biopsy contained, on an average, 16 glomeruli, and a portion of tubular tissue, interstitial tissue and vessels. Detailed studies on the significance of sampling error have not yet been made on renal biopsy material.

In the nephrotic syndrome, renal biopsy may provide an ætiological diagnosis. The section may show normal histological findings, mild, moderate or severe chronic membranous glomerulonephritis, subacute glomerulonephritis, renal amyloidosis, lupus nephritis or diabetic glomerulosclerosis. Although there were no cases in this series of lupus nephritis or amyloidosis giving rise to the nephrotic syndrome, these diagnoses had been thought of not infrequently in the clinical assessment of the patient. The demonstration of normal tissue in a case of the nephrotic syndrome is compatible with the diagnosis of either early chronic membranous glomerulonephritis or bilateral renal vein thrombosis. The histopathological variations in the kidney in renal vein thrombosis have been reviewed by Pollak *et alii* (1956). The tissue may appear normal, simulate chronic membranous glomerulonephritis, or else reflect the parenchymal changes of venous congestion. The section may also indicate the severity of the lesion. Ten patients in this series, who had the nephrotic syndrome, had no visible histological evidence of nephritis, and with only one exception, had either spontaneous or steroid-induced diuresis. The severity of glomerular damage correlated well with the response to corticosteroids. Patients with established glomerular changes were usually resistant to treatment.

In hypertension, renal biopsy can usually confirm or exclude chronic glomerulonephritis. The possibility of error due to sampling may not allow the exclusion of chronic pyelonephritis to be made so easily. How frequently this error occurs is not known at present, but future correlation of biopsy and autopsy findings will clarify this issue. To judge by the biopsy findings in cases of hypertension, an unknown or "essential" cause is not infrequent in the younger age group.

In some cases of obscure renal disease, renal biopsy led to an unexpected diagnosis. Focal embolic glomerulonephritis was demonstrated in a patient in whom the diagnosis of subacute bacterial endocarditis had not been seriously considered. The presence of moderately severe diabetic glomerulosclerosis in a young diabetic woman who was clinically well and desired a pregnancy, modified the clinician's approach to her case. Chronic glomerulonephritis was found in a boy with symptomless proteinuria, and this finding helped the general physician in the advice he gave the child's parents. Lupus nephritis was strongly suggested by renal biopsy in a young woman who was diagnosed clinically as having pyelonephritis. A woman five months pregnant was considered clinically to have chronic glomerulonephritis. Renal biopsy disclosed normal tissue, and she progressed to term without complication.

The indications for renal biopsy will become fewer as knowledge is gained from more correlative studies of the clinical and histopathological features of renal disease by the technique of renal biopsy. Further, although renal biopsy may add a new dimension to our knowledge of renal disease, it is very likely, at first, to add confusion to our old concepts before it adds much clarification.

Summary.

Aspiration renal biopsy was performed successfully on 51 patients with a wide range of renal diseases.

Certain difficulties in technique are discussed, but in general the method is not difficult to perform, and in the present series 53 out of 59 attempts were successful.

Complications following renal biopsy were uncommon. One patient developed necrotizing papillitis and required nephrectomy. In two cases there appeared to be aggravation of a preexisting infection. The relationship between biopsy and these complications is not clear.

The clinical diagnosis was confirmed in 22 cases, compatible with the histological results in 10 cases and altered in 13 cases after biopsy, and in six neither the clinical nor the biopsy features were sufficiently characteristic to be definite.

Renal biopsy may be of value in the management of patients with the nephrotic syndrome, hypertension, and miscellaneous renal diseases. An ætiological diagnosis may be provided and the severity of the lesion assessed. Information of value in prognosis and therapy may be obtained.

It is suggested that renal biopsy has a definite but limited value in clinical practice. It is no substitute for the more usual diagnostic procedures and techniques, and must be considered in the light of these methods. It is not a short cut in the diagnosis of renal diseases. Problems arise in sampling and pathological interpretation.

Acknowledgements.

We wish to thank the honorary medical staff of the Royal Prince Alfred Hospital for allowing us to publish

details of the case histories of patients under their care, and for permission to do renal biopsies.

References.

Allen, A. C. (1951), "The Kidney: Medical and Surgical Diseases", Grune and Stratton, New York.

Alwall, N. (1952), "Aspiration Biopsy of the Kidney", *Acta med. scand.*, 143: 430.

Bjørneboe, M., Brun, C., Iversen, P., Gormsen, H., and Raaschou, F. (1952), "Two Cases of Calcinosis Renis Studied by Means of Renal Biopsy and Renal Function Tests", *J. clin. Invest.*, 31: 727.

Bjørneboe, M., Brun, C., Gormsen, H., Iversen, P., and Raaschou, F. (1952), "The Nephrotic Syndrome. Histological Changes Illustrated by Means of Biopsy of the Kidney", *Acta med. scand.*, Supplement 266: 233.

Brun, C. (1954), "Acute Anuria", Ejnar Munksgaards Forlag.

Brun, C., Gormsen, H., Hilder, T., Iversen, P., and Raaschou, F. (1953), "Diabetic Nephropathy", *Amer. J. Med.*, 15: 187.

Gormsen, H., Iversen, P., and Raaschou, F. (1955), "Kidney Biopsy in Acute Anuria", *Amer. J. Med.*, 19: 209.

Greenwald, H. P., Bronfin, G. J., and Auerbach, O. (1953), "Needle Biopsy of the Kidney", *Amer. J. Med.*, 15: 198.

Iversen, P., and Brun, C. (1951), "Aspiration Biopsy of the Kidney", *Amer. J. Med.*, 11: 324.

Jackson, G. G., Poirier, K. P., and Dallenbach, F. D. (1955), "Correlation of Histopathology and Clinical Studies in Pyelonephritis", *J. Lab. clin. Med.*, 46: 925.

Joske, E. R. A., and Stubbs, J. L. (1957), "Aspiration Biopsy of the Kidney in Systemic Lupus Erythematosus", Med. J. Aust., 1: 347.

Kark, R., Muehrcke, R., Pirani, C., and Pollak, V. (1955), "The Clinical Value of Renal Biopsy", *Ann. intern. Med.*, 43: 807.

Kark, R., and Muehrcke, R. (1954), "Biopsy of Kidney in Prone Position", *Lancet*, 1: 1047.

Kipnis, G., Jackson, G., Dallenbach, F., and Schoenberger, J. (1955), "Renal Biopsy in Pyelonephritis", *Arch. intern. Med.*, 95: 445.

Lister, L. M., and Baker, R. D. (1954), "Needle Biopsy of the Kidney in the Diagnosis of Disseminated Lupus Erythematosus", *Amer. J. Med.*, 17: 851.

Major, R. H. (1954), "Bright's Disease" in "The History and Conquest of Common Diseases": 157.

Muehrcke, R., Kark, R., and Pirani, C. (1955), "Technique of Percutaneous Renal Biopsy in the Prone Position", *J. Urol. (Baltimore)*, 74: 267.

Muehrcke, R. C., Kark, R. M., and Pirani, C. L. (1955), "Biopsy of the Kidney in the Diagnosis and Management of Renal Disease", *New Engl. J. Med.*, 253: 537.

Muehrcke, R., Kark, R., Pirani, C., and Schoenberger, J. (1954), "Serial Kidney Biopsy Studies in Patients with the Nephrotic Syndrome", *J. Lab. clin. Med.*, 44: 901.

Muehrcke, R., Kark, R., Pirani, C., Pollak, V., and Joske, R. (1956), "Discussion on Renal Biopsy", *Proc. roy. Soc. Med.*, 49: 227.

Muehrcke, R., Kark, R., Pirani, C., and Pollak, V. (1957), "Lupus Nephritis", Williams & Wilkins Co.

Parrish, A., and Howe, J. (1953), "Needle Biopsy as an Acid in Diagnosis of Renal Disease", *J. Lab. clin. Med.*, 42: 152.

Parrish, A., and Howe, J. (1955), "Kidney Biopsy", *Arch. inter. Med.*, 96: 712.

Pollack, V. E., Kark, R. M., Pirani, C. L., Shapter, H. A., and Muehrcke, R. C. (1956), "Renal Vein Thrombosis and the Nephrotic Syndrome", *Amer. J. Med.*, 21: 496.

Pollack, V. E., Pirani, C. L., Kark, R. M., Muehrcke, R. C., Freda, V., and Nettle, J. (1956), "Reversible Glomerular Lesions in Toxæmia of Pregnancy", *Lancet*, 2: 59.

Ross, J. H., and Ross, I. P. (1957), "The Value of Renal Biopsy", *Lancet*, 2: 559.

Taft, H., Finckh, E., and Joske, R. (1954), "A Biopsy Study of the Kidney in Diabetes Mellitus", *Aust. Ann. Med.*, 3: 189.

Zelman, S. (1954), "Fatal Hæmorrhage Following Needle Biopsy in Uræmia", *J. Amer. med. Ass.*, 154: 997.

Legends to Illustrations.

Figure I.—Case I: Normal glomerulus. The specimen contained 18 glomeruli. (Hæmatoxylin and eosin stain, × 300.)

Figure II.—Case II: Diffuse thickening of glomerular filtration membrane. (Hæmatoxylin and eosin stain, × 300.)

Figure III.—Case V: Chronic sclerosing glomerulonephritis. Two glomeruli are obliterated and a third shows advanced glomerulitis with capsular adhesions. The tubules related to these glomeruli are atrophic. (Hæmatoxylin and eosin stain, × 75.)

Figure IV.—Case XI: Focal glomerulitis with capsular adhesions of the type seen in lupus nephritis. (Hæmatoxylin and eosin stain, × 300.)

BLACK LIVER JAUNDICE DIAGNOSED BY NEEDLE BIOPSY.

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The first cases of black liver jaundice were independently reported by Dubin and Johnson (1954) and by Sprinz and Nelson (1954). The condition was characterized by intermittent or persistent non-hæmolytic jaundice due to an elevation of both direct and indirect reacting serum bilirubin, and by the deposition of a dark granular pigment, as yet unidentified, in the hepatic cells. Dubin (1958) has recently reviewed 50 cases and now favours the name chronic idiopathic jaundice, or alternatively the Greek term suggested by Bynum (1957)—maverohepatic icterus—but we prefer the Anglo-Saxon equivalent, namely, black liver jaundice. Black liver jaundice has not previously been recorded in Australia, and although the general incidence is rare, knowledge of its unique features should facilitate the diagnosis of other cases. In our patient diagnosis was made by needle aspiration biopsy of the liver, unnecessary surgery being avoided and a good prognosis given.

Report of a Case.

The patient, a Hungarian male, aged 30 years, was admitted to the Royal Melbourne Hospital in January, 1950, with acute appendicitis and appendicectomy was performed. On his admission to hospital there was slight jaundice. Neither the liver nor the spleen was enlarged. Jaundice had been first noted when he was aged 18 years, and since then he had suffered from several attacks, each lasting several days. The scleræ were yellow for long periods, but the skin had been clearly yellow only once. There was no pruritus, but during attacks he was anorexic and the urine was dark. His general health was otherwise good and he worked hard. He was an only child, and there was no parental history of jaundice and no history of blood transfusion, or of exposure to infectious hepatitis or to hepatotoxins. His diet was good and his alcoholic intake not excessive. His occupations included carpet making, taxi driving and printing.

The laboratory findings on his admission to hospital are listed in Table I. The liver biopsy showed normal hepatic structure. There was slight increase in mononuclear cells in the portal tracts, and a moderate amount of granular brown pigment was present in the centrilobular polygonal cells (Figure I).

No diagnosis was made and he was discharged from hospital, the serum bilirubin level having fallen to four milligrammes per 100 millilitres. He was readmitted in September, 1957, complaining of weakness, anorexia, loss of weight, attacks of epigastric pain and flatulence for three months. Conjunctival icterus was present, the liver was palpable two fingers' breadth below the right costal margin, but the spleen could not be felt. The laboratory findings are again listed in Table I.

Liver biopsy was repeated, the biopsy core being greenish brown in colour, and the characteristic hepato-cellular pigment of black liver jaundice was recognized microscopically (Figures II and III). The patient improved and was discharged in good health, reassured that his prognosis was good.

In the second biopsy the hepatic structure was lobular. The portal tracts were normal. The striking feature was the presence of a considerable amount of dark granular pigment predominantly in the polygonal cells, but occasionally in the Kupffer cells, generally centrilobular in distribution, but also detectable as very fine particles in most of the peripheral cells. After fixation in 10% formol-saline, the granules appeared greenish-brown in colour in frozen sections, but golden-brown after fixation in Masson's solution, followed by paraffin embedding and staining with hæmatoxylin and eosin. They were up to three microns in diameter and irregular in shape. Despite gross accumulations of the granules, neither cell damage nor increased regeneration was visible. The results of examination of the pigment by various techniques are set out and compared

[1] Working with the aid of a grant from the National Health and Medical Research Council of Australia.

with the results obtained by other authors, as summarized by Dubin (1958) (Table II).

Discussion.

The differential diagnosis of chronic jaundice includes biliary obstruction, hæmolytic anæmia, chronic hepatitis and those conditions associated with a biochemical impairment of bile excretion by the liver. The results of liver function tests, hæmatological investigations and liver biopsy excluded the first three conditions.

Gilbert and Lereboullet (1901) described a number of cases of "*cholémie simple familiale*" or familial non-hæmolytic jaundice. The development of more sensitive tests for hæmolysis, liver function tests and liver biopsy have led to the clarification of Gilbert's disease. This is now defined as a familial recurrent or persistent non-hæmolytic jaundice associated with a rise only of the indirect reacting serum bilirubin, with acholuria and with normal findings to liver function tests. The liver biopsy shows either a normal appearance or some fat accumulation (Krarup and Roholm, 1941). The biochemical lesion is probably a failure of conjugation of the indirect reacting bilirubin with glucuronic acid in the hepatic cells to form the direct reacting bilirubin (Arias and London, 1957).

TABLE I.
Results of Laboratory Investigations.

Investigations.	1950.	1957.	Dubin (1958).
Serum bilirubin (milligrammes per 100 millilitres).	10→4	2·3—1·6	Normal to 19, both direct and indirect reacting bilirubin elevated.
Van den Bergh	Biphasic.	—	—
Urine bile pigment	+++	+++	+++
Urine urobilinogen	+++	+++	Variable.
Hippuric acid excretion (normal 3·5 grammes in four hours).	2·8	—	Normal.
Bromsulphthalein retention (45 minutes).	—	24%	Frequent impairment sometimes greater than 20%.
Serum alkaline phosphatase (King-Armstrong units).	7	5	Usually normal.
Cephalin flocculation (24 hours).	+	Negative.	Variable.
Plasma glutamic oxalacetic transaminase.	—	12 units.	Normal.
Prothrombin index	36%→68%	52%	Normal.
Total serum protein (grammes per 100 millilitres).	7·1	7·8	Normal.
Serum albumin (grammes per 100 millilitres).	4·2	4·8	Normal.
Serum globulin (grammes per 100 millilitres).	2·9	3·0	Normal.
Serum γ globulin (grammes per 100 millilitres).	1·7	1·1	Normal.
Serum lipids (milligrammes per 100 millilitres).	—	740	Normal.
Serum cholesterol (milligrammes per 100 millilitres).	—	185	Normal.
Hæmoglobin (grammes per 100 millilitres).	14	15·8	Normal.
Reticulocytes	<1%	<1%	Normal.
Coombs test	Negative.	—	Negative.
Red cell saline fragility test	Slight increase in fragility.	—	Normal.
Fæcal stercobilinogen (milligrammes per 100 millilitres).	60	33·8	Usually normal.

Apart from jaundice, many patients are asymptomatic, as was this patient for the first 12 years of his illness. The onset of symptoms at his admission to hospital in 1950 was precipitated by appendicitis, while the episode in 1957 was associated with mental stress; but the symptoms, namely, weakness, anorexia and attacks of epigastric pain, conformed with those frequently described in black liver jaundice. Other symptoms and signs frequently found (Dubin, 1958) include vomiting, mild fever, slight enlargement and tenderness of the liver, and dark urine. The fæces are usually normal in colour, and pruritus does not occur. Patients do not appear seriously ill, the jaundice diminishes over a few days, and the condition is not associated with any decrease in the life span or with progressive liver disease; some patients in their seventies have had lifelong attacks of jaundice (Bartholomew *et alii*, 1957). Attacks are precipitated by intercurrent infections, dietary indiscretions, operations, pregnancy, psychic and other stresses. They are stated to be less frequent and severe in later life. Abortions and fœtal abnormalities are frequent when pregnancy occurs in females with this condition (John and Knudtson, 1956; Bartholomew *et alii*, 1957; Dubin, 1958).

TABLE II.
Staining Reactions of Hepatocellular Pigment.[1]

Technique.	Result.	Dubin (1958).
Gmelin	Negative.	Negative.
Stein	Negative.	Negative.
Prussian blue	Negative.	Negative.
Schariach R	Negative.	Variable.
Sudan Black B	Negative (30 minutes' staining).	Positive (with prolonged staining).
Acid fastness	Negative.	Variable.
Periodic acid-Schiff	Negative.	Variable.
Diamine silver reduction	Positive.	Positive.
Basic dyes: methylene blue, Sevki Giemsa, Mallory's basic fuchsin	Positive.	Positive.
Schmori's ferric ferricyanide	Positive.	Positive.
Peroxide bleaching	Positive (10%, 30 volumes, 24 hours).	Positive.
Fluorescence (violet and ultra-violet light)	Dull brown.	Dull brown.
Polarized light	Isotropic.	Isotropic.

[1] The Schariach R stain was performed in frozen sections previously fixed in 10% formol-saline. The other techniques were performed on sections from tissue fixed in Masson's solution, paraffin embedded and five microns thick. In general the stains advocated by Pearse (1954) were used.

It was clear from the clinical, biochemical and histological features that this patient did not have Gilbert's disease, but rather black liver jaundice, as described by Dubin and Johnson (1954) and by Sprinz and Nelson (1954), and reviewed by Dubin (1958). Black liver jaundice occurs predominantly in males, and the onset of jaundice is insidious or acute; it is usually first noted during the second or third decade of life, but appears at any age. Occurrence in siblings has been recorded once (John and Knudtson, 1956), while Dubin (1958) noted a familial history of jaundice in 11 of another 37 cases. There is no clear racial or geographical distribution.

The results of laboratory investigations occurring in black liver jaundice (Dubin, 1958) are listed in Table I. The lowered prothrombin index and impaired benzoic acid excretion in this patient were atypical features.

The gall-bladder can sometimes be faintly visualized by intravenous cholecystography if a double dose of intravenous dye is given (Stein, 1955; John and Knudtson, 1956; Brown and Shnitka, 1956). No evidence of increased hæmolysis has ever been detected, even with the use of radiochromium techniques (Dubin, 1958).

Diagnosis is confirmed by liver biopsy, when virtually normal hepatic structure combined with hepatocellular pigmentation is found having a characteristic distribution and appearance (Figures II and III). A considerable increase in intracellular pigmentation occurred in the seven-year period between the two liver biopsies (Figures I and II). At the first biopsy only a few centrilobular cells contained pigment despite the attacks of jaundice over the previous 12 years; possibly early in the disease pigment is not observed in the liver specimen. However, Dubin (1958) records no significant change in hepatic pigmentation in serial biopsies, but the greatest interval between two biopsies in his series was four years.

Dubin (1958) states that "an awareness of this disease and the use of needle biopsy should eliminate unnecessary operations" and "the danger of unnecessary exploratory laparotomy can be measured by the fact that this procedure was performed in 31 of the 50 cases in this series". Nevertheless, he records the occurrence of coincidental gall-stones in five of the 50 cases, but no case of biliary obstruction occurring as a complication. At laparotomy and autopsy the liver is described as slaty-grey, greenish-

black, and black in colour. The liver biopsy specimen itself, as in our case, may be noticeably discoloured.

Elucidation of this condition requires identification of the pigment in the hepatic cells. Attempts to dissolve the pigment from the liver at autopsy have failed (Dubin and Johnson, 1954). To date, histochemical characterization has not been successful.

Positive staining reactions with Oil Red O in fresh tissue (John and Knudtson, 1956) and Sudan Black B in paraffin-embedded tissue (Brown and Shnitka, 1956) support the suggestion that the pigment is lipofuscin, i.e. an oxidized unsaturated fat. However, with our material fixed in Masson's solution and embedded in paraffin, the pigment moiety was retained, yet failed to take up lipid stains. The pigment is insoluble in fat solvents such as alcohol, ether, acetone and chloroform (Dubin and Johnson, 1954; Sprinz and Nelson, 1954; Brown and Shnitka, 1956; Bartholomew *et alii*, 1957). The granules are coarser and more profuse than typical lipofuscin granules, and the dull brown fluorescence is not characteristic of this substance (Pearse, 1954). The presence of a protein matrix was demonstrated by Brown and Shnitka (1956). Variations in the staining properties of the pigment are probably due to the techniques used, but may be due to variations in the composition of the matrix or the pigment itself.

Bynum (1957) found melanuria in his patient, and suggested that the intracellular pigment was melanin. Our staining reactions were consistent with melanin except for the greenish colour in the frozen section and the "positive" stain with Mallory's basic fuchsin. We did not find any evidence of melanuria in our patient. It is tempting to equate this pigment deposition to the known increase in melanin-like material in the skin, which occurs in chronic liver disease, e.g. chronic hepatitis and hæmochromatosis (Gisinger and Neumayr, 1955), and which we have observed ourselves in a case of long-standing chlorpromazine jaundice. However, skin pigmentation is not a feature of black liver jaundice.

In this condition, in which there is apparently a partial block of excretion of direct reacting bilirubin into the biliary canaliculi, the pigment may be expected to be an accumulation of bile pigment or bile pigment derivatives; however, the Gmelin and Stein reactions for bile pigments were "negative", and dipyrrylmethenes have been excluded (Dubin, 1958, quoting Sherlock). Nevertheless, it is possible that a highly polymerized and insoluble pigment is formed in the course of hæmoglobin breakdown and deposited in the liver cells, and such pigments may not necessarily give the classical reaction to histochemical tests for bile pigment.

The features of black liver jaundice suggest that there is a familial metabolic defect involving the natural excretion of bilirubin and urobilinogen by the hepatic cells, which also involves the excretion of bromsulphthalein and cholecystography media. It is probable that the pigment accumulation represents deposits of a naturally occurring metabolite whose excretion is similarly impaired.

Summary.

1. A case of black liver jaundice—fluctuating hyperbilirubinæmia associated with a characteristic pigment deposit in the hepatic cells — is described.

2. Atypical biochemical features of the case included a lowered prothrombin index and impaired hippuric acid excretion.

3. Diagnosis by needle aspiration biopsy of the liver avoided surgery.

4. Despite increase in the deposit of pigment as assessed in the two liver biopsies seven years apart, the patient was discharged from hospital with a good prognosis.

5. While on theoretical grounds the pigment might be derived from hæmoglobin breakdown, the histochemical reactions of the pigment were suggestive of a highly insoluble polymerized material similar to melanin or a lipofuscin.

Acknowledgements.

We wish to thank our colleagues, Dr. Sara Weiden and Dr. Ian Mackay, for their assistance in the investigation and documentation of this case.

References.

Arias, I. M., and London, I. M. (1957), "Bilirubin Glucuronide Formation in Vitro: Demonstration of a Defect in Gilbert's Disease", *Science*, 126: 563.

Bartholomew, L. G., Dearing, W. H., and Baggenstoss, A. H. (1957), "Jaundice Associated with Lipochrome Pigmentation of the Liver. (Dubin-Johnson Syndrome)", *Gastroenterology*, 33: 302.

Brown, N. L., and Shnitka, T. K. (1956), "Constitutional Non-Hemolytic Jaundice with 'Lipochrome' Hepatosis. (Dubin-Sprinz Disease)", *Amer. J. Med.*, 21: 292.

Bynum, W. T. (1957), "Mavero-Hepatic Icterus (Black Liver Jaundice)", *Gastroenterology*, 33: 97.

Dubin, I. N. (1958), "Chronic Idiopathic Jaundice", *Amer. J. Med.*, 24: 268.

Dubin, I. N., and Johnson, F. B. (1954), "Chronic Idiopathic Jaundice with Unidentified Pigment in Liver Cells; A New Clinicopathologic Entity with a Report of 12 Cases", *Medicine*, 33: 155.

Gilbert, A., and Lereboullet, P. (1901), *"La cholémie simple familiale"*, *Sem. méd. (Paris)*, 21: 241.

Gisinger, E., and Neumayr, A. (1955), *"Zur Frage der Hautpigmentierung bei Leberzirrhosen und Hämochromatosen"*, *Wien. Z. inn. Med.*, 36: 107.

John, G. G., and Knudtson, K. P. (1956), "Chronic Idiopathic Jaundice", *Amer. J. Med.*, 21: 138.

Krarup, N. B., and Roholm, K. (1941), *"Leberbiopsie bei Icterus intermittens juvenalis"*, *Klin. Wschr.*, 20: 193.

Pearse, A. G. E. (1954), "Histochemistry: Theoretical and Applied", Churchill, London.

Sprinz, H., and Nelson, R. S. (1954), "Persistent Non-Hemolytic Hyperbilirubinæmia Associated with Lipochrome-like Pigment in Liver Cells: Report of Four Cases", *Ann. intern. Med.*, 41: 952.

Stein, Y. (1955), "Chronic Idiopathic Jaundice with Unidentified Pigment in Liver", *Gastroenterology*, 29: 1087.

Legends to Illustrations.

Figure I.—Male, aged 30 years, with black liver jaundice. Liver biopsy 12 years after initial onset of jaundice, showing small amount of centrilobular pigment. (Hæmatoxylin and eosin stain, ×100.)

Figure II.—Same patient as in Figure I. Liver biopsy 19 years after initial onset of jaundice, showing considerable increase in the amount of centrilobular pigment. (Hæmatoxylin and eosin stain, ×100.)

Figure III.—Liver biopsy as in Figure II. High-power view of pigment granules in polygonal cells in the centre of the lobule. (Hæmatoxylin and eosin stain, ×600.)

THE OCCURRENCE OF EPISODES OF IMMUNIZATION IN PREGNANCY ASSOCIATED WITH Rh HÆMOLYTIC DISEASE OF THE NEW-BORN.[1]

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and

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During the past seven years, in our studies on hæmolytic disease of the new-born we have carried out routine titrations of antibodies found in pregnant mothers' serum (Kelsall and Vos, 1952; Kelsall, Vos, Kirk and Shields, 1957). In this way we have often been able to note the first appearance of Rh antibodies in a particular patient.

We began to use the phrase "episode of immunization" whenever antibodies first appeared in a patient. Once the antibodies had been found, the next step was to follow their subsequent behaviour by frequent titrations in the remainder of the pregnancy. It soon became evident that

[1] Read at a meeting of the Section of Pædiatrics, Australasian Medical Congress (B.M.A.), Tenth Session, Hobart, March 1 to 7, 1958.

ILLUSTRATIONS TO THE ARTICLE BY D. J. DELLER, V. J. McGOVERN AND RALPH READER.

FIGURE I.

FIGURE II.

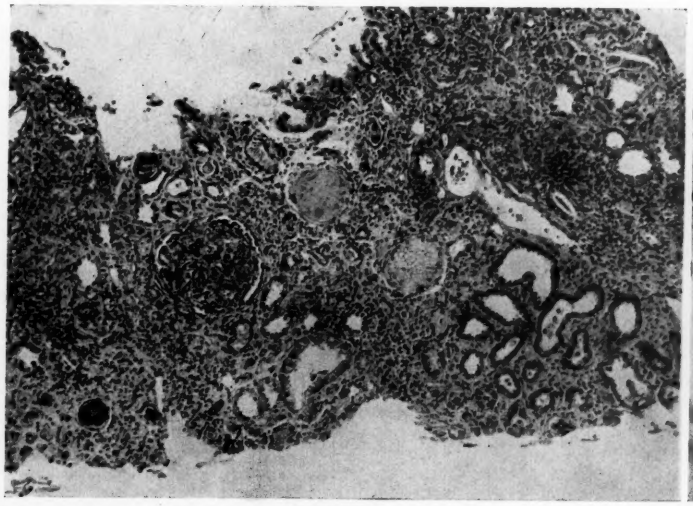


FIGURE III.

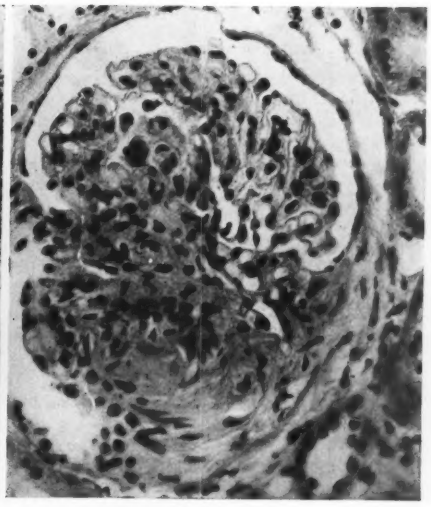
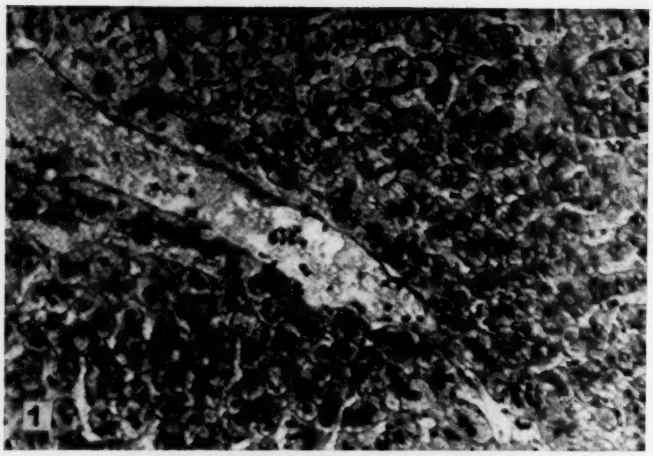
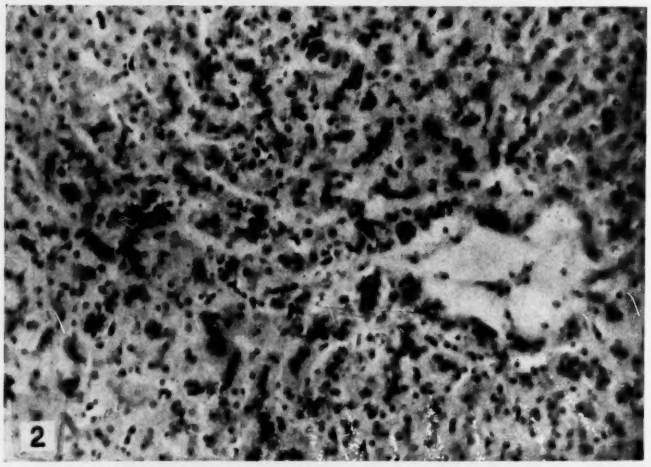
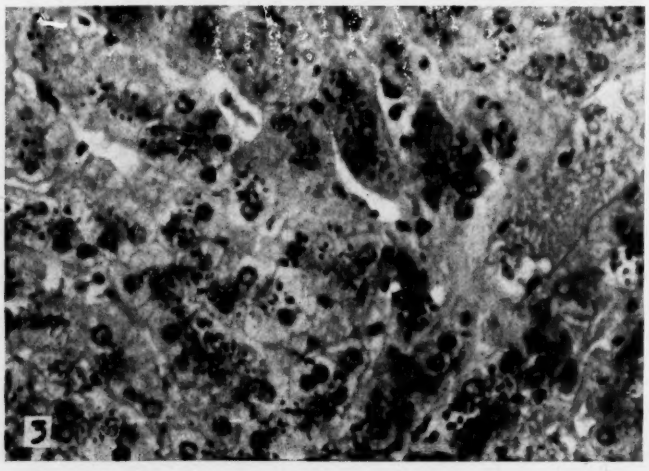


FIGURE IV.

ILLUSTRATIONS TO THE ARTICLE BY L. I. TAFT AND E. EARLE.







more than one episode could occur during a pregnancy, and that the resulting immunization could be of minor or major magnitude.

The antibody behaviour patterns are numerous and varied, and it is proposed to discuss some of the typical findings, together with the subsequent final results of the pregnancies. It is upon these findings that we are not only able to give a prognosis for that particular pregnancy, but often also to indicate the outlook for later pregnancies.

In striving for the same objective, other workers have attempted to obtain their prognostic information by assessment of the severity of immunization in previous pregnancies which had resulted in death or disease of the former infant. Walker *et alii* (1957) have evolved "percentage risk" values depending upon the outcome of the previous pregnancies, and have reluctantly admitted that in cases in which the father is homozygous (DD) and there has been a previous stillbirth or seriously affected baby, premature induction of labour is the proper course of treatment. The weakness of such an argument is that a serious case must first occur before any attempt is made to save the subsequent infant by premature induction of labour, and that it allows the antibodies to soar in an early pregnancy, thereby risking not only that infant, but also subsequent ones; on the other hand, an assessment based on antiglobulin titre gives a better chance of saving that infant as well as those following later.

It is perhaps best if we quote examples taken from 66 cases in which we have studied women who have had two or more pregnancies under our care, as well as from some 500 others in which the relevant information is available.

Fortunately, in 95% of Rhesus incompatible pregnancies no episode of immunization occurs at all. The woman goes from the beginning to the end of pregnancy without the appearance of antibodies. Moreover, we have only twice found antibodies in gravid primiparæ, and in each case the woman had been immunized by a previous incompatible blood transfusion. We have, however, found antibodies in the serum of primiparæ in the puerperium on several occasions, a finding which inclines us to the belief that the separation of the placenta may often be associated with an episode of immunization. This view is strengthened in other cases by finding potent antibodies very early in a second pregnancy when they have been absent from the patient's serum as a primigravida. Although it must be admitted that an episode could theoretically have occurred early in the second pregnancy, there would hardly be time enough in most instances to attain the titres noted, and in our cases there were no proven definite episodes in the first trimester. However, we have cases on our records in which antibodies have been found early in a second pregnancy in which the first baby had been Rh-positive and the response to the Coombs test negative at his birth, and the second baby was himself Rh-negative.

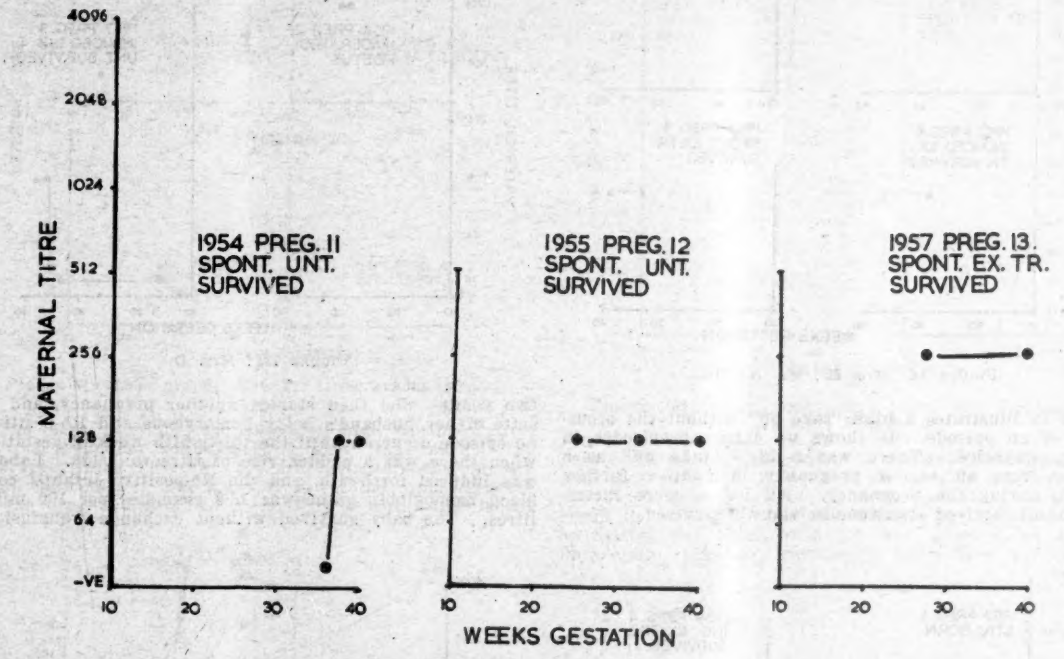


FIGURE I: Mrs. A.

More than one episode may occur in a pregnancy, and we believe that more than two may occur, though it is difficult to be sure where one finishes and another begins unless a definite plateau can be demonstrated between episodes.

Some episodes appear to be more devastating in their results than others. Occasionally the rise in titre is small and in other cases the titre rises dramatically in a short space of time; it is this latter type which results in some of the most serious cases. Possibly the amplitude of antibody response is related to the mass of fœtal red cells finding their way into the mother, while the varying ability to form antibodies from unit dosage of antigen must also have some bearing on the response.

The behaviour of no two cases is identical, though various patterns are broadly recognizable, as follows.

Figure I[1] illustrates low antibody "take off" in a pregnancy without a subsequent episode in that pregnancy. There is a large number of cases in which an episode occurred in an earlier pregnancy and the titre rose to an inconsequential figure, remaining at that level when the

[1] The following abbreviations are used in the illustrations: SPONT., spontaneous labour; UNT., untreated; EX. TR., exsanguinating transfusion; INDUCED L/B, induced labour; S/BORN, stillborn.

woman again appeared in her next pregnancy. No episode occurred in the latter pregnancy, even though the baby was eventually found to be Rh-positive. So mild was the infant's disease that no active treatment was required. Note the rise between twelfth and thirteenth pregnancies—suggesting, but by no means proving, that an episode of immunization occurred at the separation of the placenta.

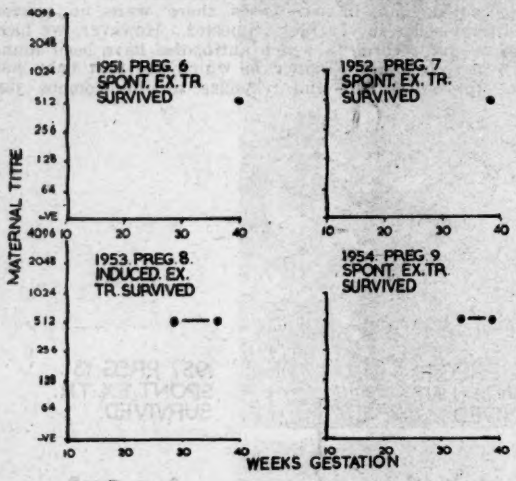


FIGURE Ia: Mrs. B.; Mr. B., D/D.

Figure Ia illustrates a high "take off" without the occurrence of an episode. It shows no apparent episodes in four pregnancies. There was a high "take off" as a residue from an earlier pregnancy, without a further episode during the pregnancy. All babies were incompatible, all received transfusions and all survived.

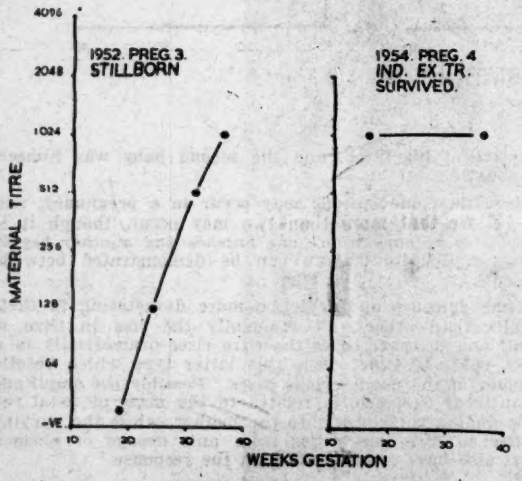


FIGURE II: Mrs. C.

Figure II shows the type of case which most workers would recognize as being suitable for premature induction of labour. They would perhaps base their prognosis upon the previous stillbirth and not upon the titre level. But they also, like us, could be misled if the father was heterozygous and the infant Rh-negative. All such Rh-positive infants will require exchange transfusion; but any further episode of immunization will make the need for it even greater and more urgent.

Figure III demonstrates a low "take off" following a previous stillbirth. In this case the woman had a stillbirth, her antibody titre at the time being 1/1024. On our advice she did not again become pregnant until the antibody titre had fallen to low levels. We watched her titre at regular intervals after the stillbirth, and much to our surprise the titre fell very rapidly to 1/16 in a little over

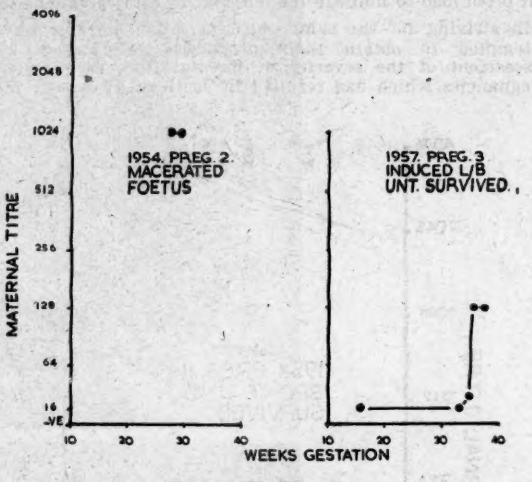


FIGURE III: Mrs. D.

two years. She then started another pregnancy, and in spite of her husband's being homozygous and Rh-positive, no episode occurred until the thirty-fifth week of gestation when there was a sudden rise of titre to 1/128. Labour was induced forthwith, and the Rh-positive infant's cord blood hæmoglobin value was 16·3 grammes per 100 millilitres. The baby survived without exchange transfusion,

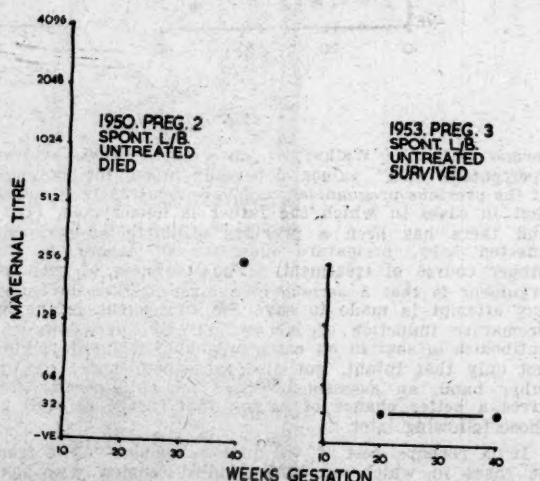


FIGURE IV: Mrs. E.

although he subsequently became jaundiced for several days. Had there been no episode at the thirty-fifth week, premature induction of labour would not have been necessary. This occurred in another case (Figure IV) in which, after the patient had lost her second infant after a spontaneous delivery at 41 weeks' gestation, the titre fell from 1/256 to 1/32, at which level it continued right through to 40 weeks in her third pregnancy without any

rise of titre. The Rh-positive infant was untreated and survived without incident. Some workers would, on the teaching of "induction after previous stillbirth", have induced labour prematurely in this latter case when in actual fact it was quite unnecessary. It will be appreciated that in cases of this nature titrations were repeated once, or if possible twice, a week during the last six weeks of pregnancy.

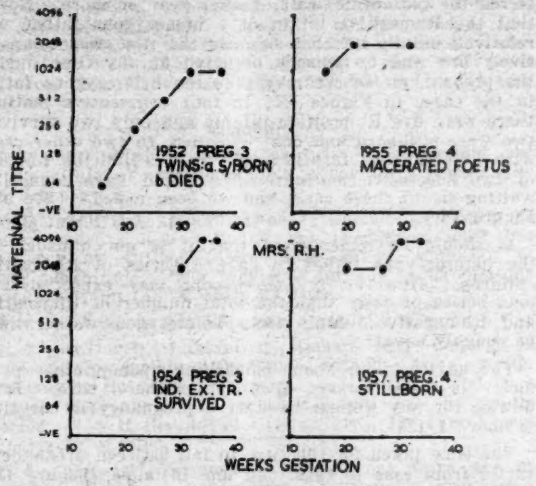


FIGURE V: Upper graphs, Mrs. F.; lower graphs, Mrs. G.

The next type of case shows a high antibody titre in one pregnancy followed by a high "take off" in the next pregnancy (Figure V). Unfortunately this picture is all too common, and it is due to the too rapid sequence of the pregnancies. The high titre of antibodies is the

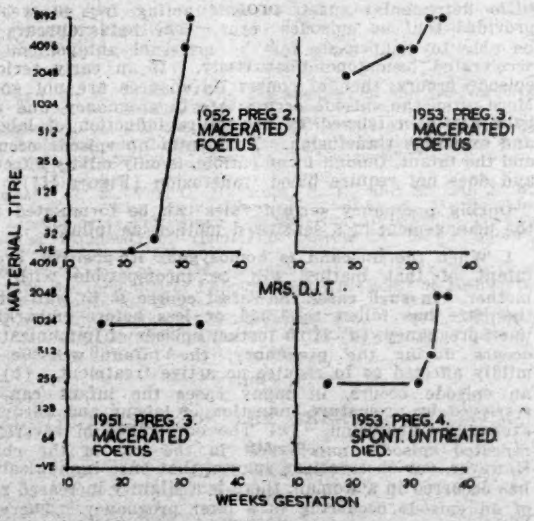


FIGURE VI: Upper graphs, Mrs. H.; lower graphs, Mrs. I.

residue from a previous pregnancy, which may have resulted in a seriously affected infant, a stillbirth, or even a mildly affected infant. If the father in a high "take off" pregnancy is homozygous, the chances for the infant's survival are indeed poor. Even if no episode of immunization occurs, the fœtus must normally endure a hostile antibody environment for the gestation period. If an episode occurs, then its chances are virtually nil.

In Figure VI are shown two cases in which premature induction of labour would also be employed by those who based their treatment upon previous history. The tragedy is that the woman may carry the infant to about 30 to 34 weeks with no rise in titre, and then the titre rises to very high levels so suddenly that there is no chance of saving the baby by premature induction of labour. We have been tempted in several recent cases to deliver the

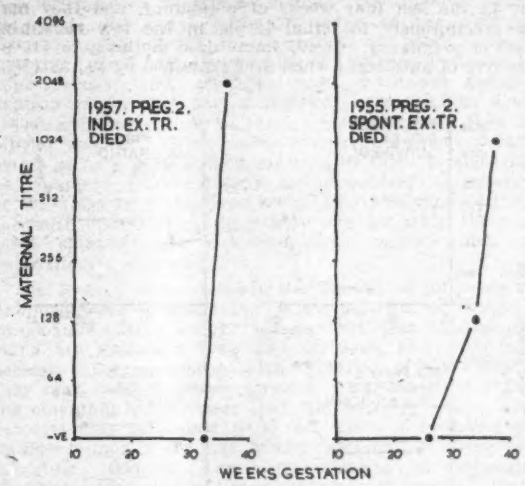


FIGURE VII: Left-hand graph, Mrs. J.; right-hand graphs, Mrs. K.

baby even earlier than 35 or 36 weeks. Sometimes this has been successful and in other cases it has not. We believe, however, that to leave the infant *in utero* will result in certain stillbirth within a short space of time; to deliver the child forthwith and perform an almost immediate exchange transfusion offers him at least a

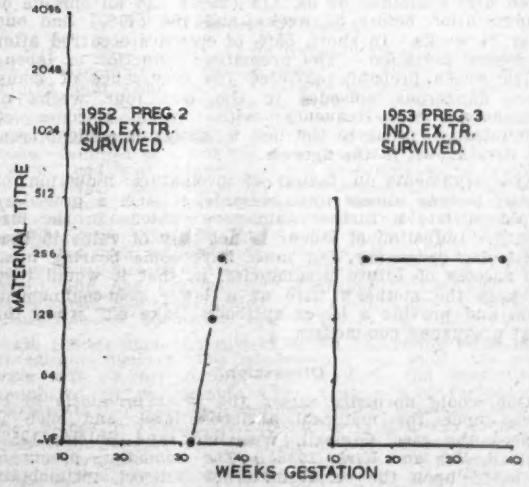


FIGURE VIII: Mrs. L.; Mr. L., D/D.

fighting chance. Those which ended in failure we have not regretted; those infants that have been saved were fortunate. We have not lightly undertaken this form of early premature induction of labour; but in some instances it has resulted in the woman's having a single surviving child after a series of tragic disappointments, and it is worthwhile under such circumstances.

It has been stated by a number of workers that if antibodies have not appeared by 34 to 35 weeks, their appearance at or after this time need occasion little or no anxiety, since they will have insufficient time to rise to dangerous levels. Hardly had we read one such publication (Bourke, 1955) than we lost an infant at term from severe erythroblastosis, when the mother had, on several occasions prior to 36 weeks, shown no trace of antibodies in her serum (Figure VII). Contrary to popular belief, antibodies frequently appear for the first time in the last four weeks of pregnancy, and they may rise precipitously to lethal levels in the few remaining weeks of pregnancy. Of 409 immunized mothers, 75 (18%) were free of antibodies when first examined by us; 33 (8%)

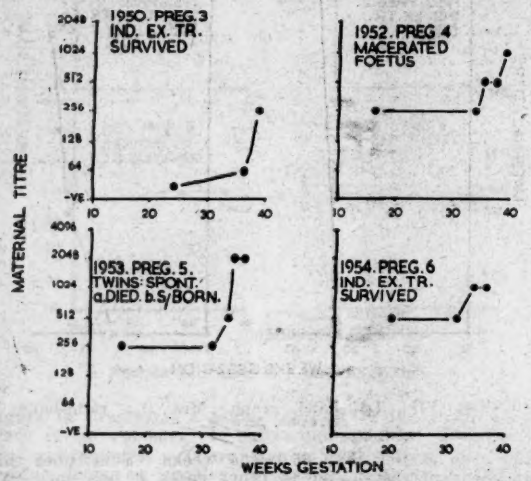


FIGURE IX: Mrs. M.

developed antibodies before 34 weeks of gestation had been completed; and 42 (10%) developed them after this time. Of the 334 (72%) who already had antibodies when first examined by us, 113 (25%) had an episode of immunization before 34 weeks, and 196 (45%) had one after 34 weeks. In short, 55% of episodes occurred after 34 weeks' gestation. The premature induction of labour at 36 weeks probably obviated the occurrence of many more dangerous episodes in the last four weeks of pregnancy. The frequency with which episodes of immunization occur in the last trimester is evident from the data shown in the figures.

The arguments in favour of premature induction of labour become almost unanswerable, if such a procedure would obviate a further dangerous episode in the last month. Induction of labour is not only of value in that particular pregnancy, but must have some bearing upon the success of future pregnancies, in that it would tend to keep the mother's titre at a lower post-confinement level and provide a lower antibody "take off" when the next pregnancy commences.

Discussion.

One would normally expect the fœtal prognosis to be based upon the maternal antibody level, and such is indeed the case (Kelsall, Vos, Kirk and Shield, 1957: Kelsall, Vos and Kirk, 1958). The immediate prognosis is based upon the serial maternal indirect antiglobulin titres during pregnancy and at the time of delivery; the remote prognosis for later pregnancies is based upon the antibody titre in this pregnancy, its level between this and the next pregnancy, its "take off" level during the later pregnancy, the number of episodes which occur and the ultimate level in the subsequent pregnancy.

We are frequently asked by distrated couples: "What are we to do? We have lost most of our previous infants from hæmolytic disease and we badly want another baby. Each of the last pregnancies has resulted in a stillbirth. Do we stop, or do we risk another fruitless pregnancy?"

Whenever we encounter this problem, we make no comment until we have ascertained the mother's present antibody titre and have determined whether the father is homozygous or heterozygous. The arguments are best illustrated by examples—which reveal that there are many traps for the unwary. In the case shown in Figure VIII we did not advise this pregnancy and would have preferred the patient to wait another year or more. Notice that the Rh-positive infant of a homozygous father was relatively mildly affected, because the titre was comparatively low and no episode occurred at any time during the pregnancy. Or we may take the heterozygous father in the cases in Figure IX; in four consecutive matings there were five Rh-positive infants and only two survived, two were still-born and one twin died. In two other cases with heterozygous fathers there were stillbirths in each of two successive matings. We would have counselled waiting in all these cases had we been asked. (See also Figure VI.)

It should be remembered that it is not unusual for the heterozygous father to have a series of Rh-positive children. However, in general one may expect over a long series of cases that the total number of Rh-positive and Rh-negative infants from heterozygous fathers will be roughly equal.

The advice given about embarking upon another pregnancy is based largely upon the mother's titre. It is unwise for any woman to start a pregnancy if her titre is above 1/128.[1]

The time taken for the titre to fall between pregnancies varies from case to case. In one instance (Figure III) it fell from 1/1024 to 1/32 in two years, whereas in other cases there may be no appreciable fall in five years.

The mating of a homozygous father with a woman whose antibody titre is high (1024 or more) is almost certain to result in a still-born or severely affected infant, because the full force of antibody is acting for the whole 40 weeks on the infant, even if no further episode occurs. If, however, the pregnancy begins with a low "take off" of 1/64 or less, we find that a titre of this degree has little detrimental effect even if acting for 40 weeks, provided that no episodes occur. The fœtus appears to be able to compensate for the maternal antagonism by accelerated hæmatopoietic activity. If an early serious episode occurs, then of course its chances are not good. More often the episode occurs late in pregnancy, and the baby can be retrieved by premature induction of labour and exchange transfusion. Frequently no episode occurs, and the infant, though incompatible, is only mildly affected and does not require blood transfusion (Figure III).

During pregnancy certain rules can be formulated for the management of a sensitized mother, as follows.

1. When the husband is homozygous Rh-positive, every infant of that mating will be incompatible with its mother. In such cases the safest course is to wait until the titre has fallen to 1/128 or less before embarking upon pregnancy. (*a*) If no further episode of immunization occurs during the pregnancy, the infant will be so mildly affected as to require no active treatment. (*b*) If an episode occurs, in many cases the infant can be retrieved by premature induction of labour and adequate exchange transfusion. (*c*) The occurrence of severe or repeated episodes may result in the loss of the child. However, our observations suggest that once immunization has occurred in a woman, there is a slightly increased risk of an episode occurring in a later pregnancy. There is also some reason to suppose that one episode of immunization predisposes towards further episodes in that or in later pregnancies. However, if the ab-initio titre is low enough, she has a good chance of going right through the pregnancy without another episode and bearing a virtually unaffected child. We have, however, noted the association of episodes with manipulations such as versions, and

[1] It must be emphasized that this figure is that determined in our own laboratory. Other laboratories using slightly modified titration techniques may have a different level.

would suggest that these be kept to a minimum in heteroppecific pregnancies.

2. With the heterozygous husband there is an equal chance that the baby will be compatible with its mother and therefore unaffected. If the mother is a young woman, she may insist upon the rapid repetition of pregnancies until she bears an unaffected Rh-negative infant. With each incompatible pregnancy her titre may become higher, and the children are severely affected and may die; but she is compensated by the eventual arrival of the compatible infant. The approach of the older women is not quite so flamboyant. They are not prepared to risk repeated losses for the sake of a possible unaffected baby. They, then, must otherwise be prepared to wait until their titre has fallen to a safe "take off" level before starting another pregnancy.

Summary.

Ante-natal antibody titrations have been carried out in our clinic at every available opportunity during the last seven years.

It is found that immunization of the mother occurs as one or more episodes during the pregnancy, and that the resulting antibody titres may be of minor or of major magnitude. The prognosis for the fœtus depends very largely on the Rh-antibody titre.

The following conclusions have been stated:

1. A previously immunized woman may undergo a further incompatible pregnancy without any episode occurring in the later pregnancy. (*a*) If the initial titre in such a pregnancy is low, the infant will be mildly affected. (*b*) If the initial titre is high, the infant may be severely affected.

2. A previously immunized woman may have one or more episodes in a subsequent incompatible pregnancy. The outcome for the fœtus will depend upon (*a*) the number of episodes, (*b*) the rise of titre and (*c*) the duration of a high titre of antibodies.

3. Antibody titres may fall between pregnancies, and sufficient time must be allowed for this to happen. A sensitized woman mated to a homozygous man has a much better chance of having a surviving infant if her titre is low at the beginning of pregnancy.

4. More episodes of immunization occur after 34 weeks of gestation than before.

References.

BOURKE, G. M. (1955), "The Management of the Rh-Negative Mother in General Practice", MED. J. AUST., 2: 1095.

KELSALL, G. A., and VOS, G. H. (1952), "The Antibody Titre in Maternal and Infant's Serum as an Indicator for Treatment in Hæmolytic Disease of the Newborn", MED. J. AUST., 1: 349.

KELSALL, G. A., VOS, G. H., KIRK, R. L., and SHIELD, J. W. (1957), "The Evaluation of Cord-blood Hemoglobin, Reticulocyte Percentage and Maternal Antiglobulin Titre in the Prognosis of Hemolytic Disease of the Newborn", *Pediatrics*, 20: 221.

KELSALL, G. A., VOS, G. H., and KIRK, R. L. (1958), "The Case for the Induction of Labour in the Treatment of Hæmolytic Disease of the Newborn", *Brit. med. J.*, 2: 468.

WALKER, W., MURRAY, S., and RUSSELL, J. K. (1957), "Stillbirth Due to Hæmolytic Disease of the Newborn", *J. Obstet. Gynæc. Brit. Emp.*, Volume 64.

ACUTE TORSION OF THE GREATER OMENTUM.

By A. RUMORE,
Sydney.

ACUTE, complete torsion of the greater omentum resulting in circulatory obstruction and strangulation would appear to be quite uncommon as reviewed in the literature. The first case was recorded by Marebette in 1851, and since then approximately 250 cases have been recorded (Boa, 1955). However, it appears certain that many cases have not been recorded and that the condition is much more common than these figures would indicate. Little, if any, reference to this condition can be found in many of the standard textbooks of surgery.

Ætiology.

Acute torsion of the greater omentum is classified into two main groups: (i) Unipolar torsion, also known as idiopathic or primary omental torsion, in which the greater omentum hangs freely in the abdominal cavity with no apparent pathological features, or in which there is only some increase in density of the dependent portion such as localized fibrosis or tumour. (ii) Bipolar torsion, in which the distal dependent edge of the omentum becomes adherent to the inguinal or pelvic regions, forming a fixed axis about which the omentum rotates. In approximately 50% of these cases the lower point of fixation is an inguinal or femoral hernia (Boa, 1955).

The unipolar variety of torsion is much rarer than the bipolar variety. The greater omentum may twist as a whole or as a part or as a strand; all three torsions may be complete (strangulated) or incomplete (congested), or they may be primary or secondary. The condition may be acute or subacute, and there are probably recurrent cases causing recurrent abdominal pains which are impossible to diagnose.

The factors which initiate the torsion in all types are unknown, and it seems that a combination of factors is responsible. Payr (1902) pointed out that the omental veins are unusually long and tortuous, and when they become engorged by the initial rotation of the omentum they may cause complete torsion. Also, the right side of the omentum hangs lower than the left side and in obese subjects may be loaded with fat. Thus it is found that torsion is mostly confined to the right half of the greater omentum. Œdema from inflammations or congestive cardiac failure may be other contributory factors. Hadda (1910) suggested that herniation of the greater omentum into a hernial sac may give rise to torsion by a "rifling effect" such as a bullet travelling along the barrel of a gun. This theory is supported by the fact that the majority of omental torsions occur in association with a hernia. Sudden jerky movements or abdominal trauma may be ætiological factors, and this fact may explain the greater incidence of torsion in males than in females. Most patients are in the age group 30 to 55 years (65%) (Etherington-Wilson, 1945).

Reports of Cases.

CASE I.—The patient was an Italian male labourer, aged 23 years. He presented with a history of severe sudden pain in the right groin and in the right iliac fossa immediately after lifting a heavy weight at work. The pain was severe and continuous, but not colicky in nature. A swelling had also suddenly appeared in the right groin. The patient had been examined at a hospital casualty department, where the "lump" had been reduced, but had soon reappeared and had subsequently disappeared on three occasions, having been pushed back by the patient, but each time it had reappeared after movement. The patient had been unable to reduce the swelling over the preceding twelve hours. The pain had prevented him from sleeping, eating or walking. He had no previous history of abdominal pain or of swelling in either groin, and had not had any vomiting or diarrhœa. His bowels had not been opened for 24 hours. There were no other relevant findings in his own or in his family history.

On examination, the patient was a tall young adult male in obvious distress. The temperature was 98°F., the pulse rate was 80 per minute and regular, and respirations numbered 18 per minute. The tongue was furred. On examination of the right inguinal region, a tender swelling two inches by two and a half inches in size was found. It was irreducible and there was no impulse on coughing. The right spermatic cord was much thickened by œdema. The left inguinal region was normal. There was some mild tenderness of the right iliac fossa. No abdominal masses were felt, and examination *per rectum* revealed no abnormality. The bowel sounds were normal and there was no abdominal distension. Examination of the urine revealed no sugar, albumin or bile.

A diagnosis of incarcerated right inguinal hernia was made and immediate exploration of the right inguinal canal was undertaken. The spermatic cord and the walls of the inguinal canal were markedly œdematous. On separation of

the structures an indirect hernial sac was found and opened. It contained a mass of œdematous, dark, strangulated greater omentum. When the greater omentum was further delivered into the wound, it was found that a small strand of greater omentum was attached to the tip of the hernial sac (Figure I). Two separate portions of the free end of the greater omentum approximately five inches in length had passed behind this thin strand and had become strangulated

Figure I.
Diagram showing a strand of the greater omentum adherent to the fundus of the hernial sac.

in the hernial sac. These two portions of the greater omentum had also undergone a complete torsion in a clockwise direction within the abdominal cavity (Figure II). It was possible to display the torsion quite clearly through the inguinal incision, and approximately five inches of strangulated greater omentum were removed. The distal segment of

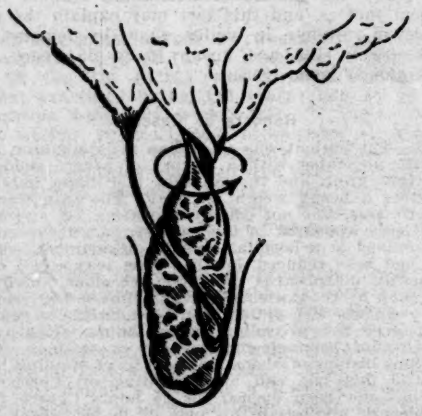


Figure II.
Diagram showing torsion of the greater omentum within the abdomen and incarceration within the hernial sac.

the greater omentum removed was similar in appearance to an acute, œdematous, gangrenous, vermiform appendix, the tip being rounded and moulded, suggesting "rifling" in the inguinal hernial sac. The hernial sac was removed and the inguinal canal repaired with stainless steel wire. No other abnormality was discovered on examination of the greater omentum. The patient made an uneventful recovery.

Case II.—The patient was an Australian, male, retired bank clerk, aged 64 years. He presented with a history of bilateral inguinal hernia in 1928. The right-sided hernia became obstructed in 1930, and at operation a bilateral repair had been performed. The hernia on the right side had recurred in 1937 and had gradually increased in size. He had worn a truss on and off for eight years, but had not worn one for the last few years. He had suffered occasional pain from the hernia after exertion, but it had always been reducible. Prior to his admission to hospital he had become constipated, had not passed a motion for two days, and at 8 a.m. on the day of admission he had strained very much at stool. While he was straining his hernia came down and became suddenly painful and for the first time he could not reduce it. The pain became increasingly severe. His medical attendant attempted without success to reduce the hernia by taxis under light anæsthesia. He was referred to hospital and was admitted at 6 p.m. The patient had not vomited, and the pain was confined to the right groin and the right

Figure III.
A twist demarcates the partly strangulated distal area. The fibrous band is shown in the area of the twist.

iliac fossa. He had experienced mild intermittent claudication in the right limb for some years. There were no other relevant findings in his own or in his family history.

On examination the patient was an elderly man in obvious distress. The temperature was 98°F., the pulse rate was 86 per minute and regular, and respirations numbered 16 per minute. The blood pressure was 170 millimetres of mercury systolic and 100 millimetres of mercury diastolic. In the right inguinal region there was an irreducible tender swelling three inches by one and a half inches in size. There was no impulse on coughing. There was definite tenderness and moderate guarding in the right iliac fossa. No abdominal masses were felt, and examination *per rectum* revealed no abnormality. The bowel sounds were normal and there was no abdominal distension. There was some wasting of the tibialis anterior muscle of the right leg, which caused no obvious disability. Examination of the urine revealed no sugar, albumin or bile. The hæmoglobin value was 15·6 grammes per 100 millilitres. A diagnosis of incarcerated right inguinal hernia was made, and an immediate exploration of the right inguinal canal was undertaken. The spermatic cord and the walls of the inguinal canal were markedly œdematous. The hernia had by this time reduced

itself and a large, thickened, indirect sac was present. The hernial sac was empty, but on further examination the greater omentum was delivered from the abdomen into the wound. The findings were as described in the pathologist's report and as seen in Figures III and IV. The report of the pathologist (Dr. E. Hirst) was as follows:

> The specimen was a roughly conical piece of omentum 15 cms. in maximum length. The base was flattened and measured 5 cms. in maximum width. The tip of the cone corresponded to the distal end of the specimen.
>
> Situated 6 cms. from the tip there was a clockwise twist which separated the specimen into two parts. The distal part was notably congested, compressed and showed a rifling effect. The twist was partly maintained by a thin round strong elastic fibrous band. The proximal part showed no discoloration of the external surface.

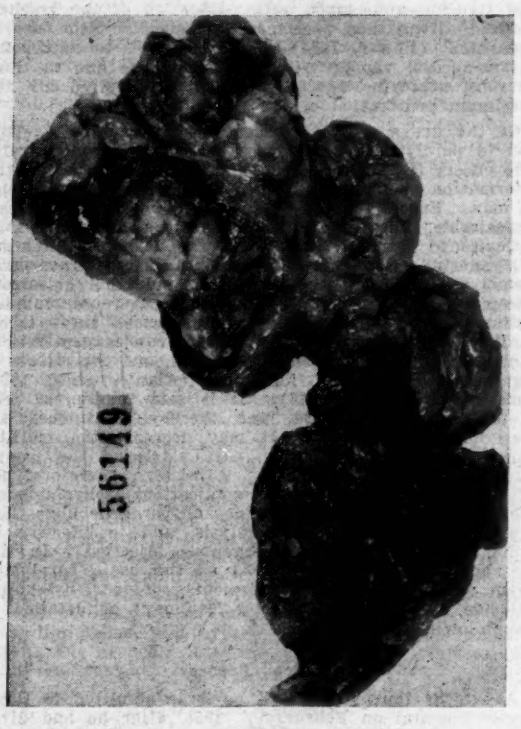


FIGURE IV.

Cut surface of the partly untwisted specimen showing one of the firm nodules. The thin adhesions are also seen.

Thin fibrous adhesions bound adjacent areas, each to the other, in both parts of the specimen.

Three very firm ovoid nodules were palpable in the distal part—the largest 2·5 × 2 × 2 cms. and the smallest 1 cm. in diameter. The cut surface of these nodules showed hæmorrhagic fat with loss of lobular pattern. The remainder of the cut surface of the distal part showed prominent vessels, and compressed, congested adipose tissue of otherwise normal lobular pattern. The cut surface of the proximal part showed normal adipose tissue.

Microscopical examination of the firm nodules showed extremely dilated veins. The walls of the arteries and some of the veins were viable. In the walls of some of the veins nuclei were absent, indicating early necrosis. There were areas of hæmorrhage into the adipose tissue and nearby necrotic adipose tissue. Occasionally there were foci of neutrophils. These appearances indicated recent necrosis. Near the surface there were a few areas of granulomatous inflammation reactive to escaped fat and indicative of small areas of previous fat necrosis. The remainder of the adipose tissue of the distal part was congested. That of the proximal part was normal. Section of the fibrous band showed fibrosis with no special features.

The indirect hernial sac was removed and the inguinal canal was repaired with silk. An associated, apparently acute, vaginal hydrocele was dealt with by subtotal excision of the sac wall.

During the operation, performed under general anæsthesia, the patient developed marked hypotension, which was quickly relieved by the intravenous administration of serum albumin. The patient made an otherwise uneventful recovery.

Discussion.

As previously pointed out, the factors which initiate torsion of the greater omentum are unknown and a history of sudden jerky body movements or abdominal trauma is very infrequently obtained. However, these two patients gave a clear-cut history of a sudden strain followed immediately by the onset of acute pain and by the sudden appearance of a swelling in the right inguinal region. The rounded, pointed appearance of the distal tip of the greater omentum found in each case is suggestive of the "rifling" effect described by Hadda. Thirdly, in the first case there was adhesion of a slip of greater omentum to the tip of the hernial sac. The sudden forceful slipping of a mass of greater omentum into the hernial sac behind this band, by traction on it, would be sufficient impetus to initiate the torsion. It would appear that a combination of these three factors was the cause of the acute omental torsion in the first case.

In the second case, the marked increase in intra-abdominal pressure at stool causing the sudden forceful expulsion of a mass of greater omentum into a preexisting hernial sac seems to have initiated the torsion by the "rifling" effect.

In both of these cases there was marked œdema of the inguinal canal, and the rotation of the omentum was in a clockwise direction.

Diagnosis.

The condition of acute omental torsion is hardly ever diagnosed before operation. The great majority of cases are diagnosed as acute appendicitis. The condition, especially the unipolar variety, can be mistaken for any of the other acute abdominal emergencies. In the bipolar variety, if there are adhesions in an inguinal hernial sac, the condition is most frequently mistaken for strangulated hernia. There are certain symptoms and signs which would suggest the diagnosis of acute omental torsion. The patient, probably an adult male, presents with right-sided abdominal pain increasing in severity. Vomiting, abdominal distension, pyrexia and other signs of a toxic state are usually absent, and tenderness and rigidity are also absent. There may be a history of sudden jerky body movement or of abdominal injury, and frequently a hernial scar or sac may be present. There may be a reducible or an irreducible swelling in the inguinal region. A tender doughy mass in the mid-line of the abdomen or in the right iliac fossa is an important suggestive sign.

Treatment.

As the diagnosis is in doubt in practically all cases, exploration by a right lower paramedian or lower mid-line abdominal incision should be undertaken. The segment of strangulated greater omentum should be removed. In the cases reported in this paper, it was fortunate that a large portion of the greater omentum was able to be delivered through the inguinal incision and the torsion demonstrated quite clearly. However, as Boa points out, in the operation for strangulated hernia, if the sac contains gangrenous omentum and an obvious point of constriction cannot be demonstrated, a laparotomy should be performed as otherwise the distal portion only of an omental torsion may be resected, leaving behind the proximal portion of a bipolar torsion.

Summary.

1. Acute, complete torsion of the greater omentum, although rare, is more common than the number of reported cases would indicate.

2. The ætiology is obscure, and a combination of factors may be responsible for the torsion. In the cases reported in this communication, a sudden strain, the adhesion of a slip of greater omentum to the tip of an indirect inguinal hernial sac and the "rifling" effect of the omentum in the hernial sac combined to cause torsion and strangulation.

3. The condition is practically never diagnosed before operation. Factors which lead one to consider the diagnosis are right-sided abdominal pain in the absence of vomiting, abdominal distension, toxic signs, tenderness or rigidity, and the finding of a tender doughy mass in the mid-line of the abdomen or in the right iliac fossa. There may be a history of a sudden strain or of an abdominal injury. A hernial scar or an inguinal or femoral hernia is often present, and if a mass is present in the inguinal canal, it may be impossible to differentiate the condition from strangulated hernia.

4. The treatment is by operative interference, usually by laparotomy. In the cases reported in this paper, it was possible to demonstrate the torsion clearly, and the strangulated omentum was removed through the inguinal incision.

Acknowledgements.

I wish to thank Dr. E. Hirst, pathologist at the Kanematsu Memorial Institute of Pathology, Sydney Hospital, for his report, Dr. T. O. R. Yates, medical superintendent, Canterbury District Memorial Hospital, for permission to publish the second case, Mr. R. Money, department of photography, Sydney Hospital, for the photographs and Mr. R. B. Dunphy for the preparation of the diagrams.

References.

AIRD, I. (1957), "A Companion in Surgical Studies", E. & S. Livingstone, Edinburgh and London.

BERNATZ, P. (1956), "Unusual Conditions Simulating Acute Appendicitis", *Proc. Mayo Clin.*, 31: 53.

BOA, P. A. (1955), "Omental Torsion as a Surgical Emergency", *Brit. J. Surg.*, 43: 315.

COOPER, N. C. (1955), "Torsion of Omentum", *Lancet*, 1: 130.

ETHERINGTON-WILSON, W. (1945), "Torsion of the Great Omentum. Report of Four Cases", *Brit. J. Surg.*, 33: 142.

TILLE, R. J. (1953), "Idiopathic Segmental Hæmorrhagic Infarction of the Greater Omentum", *Ann. Surg.*, 138: 279.

WATSON, L. F. (1948), "Hernia", 3rd Edition, Mosley, St. Louis: 111.

Reports of Cases.

SEVERE TETANUS TREATED WITH d-TUBOCURARINE CHLORIDE ("TUBARINE") AND TANK RESPIRATION.

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SEVERE TETANUS carries a high mortality rate, and the commonest cause of death is stated to be respiratory failure (Garcia-Palmieri and Ramirez, 1957; Firor *et alii*, 1940; Pelloja, 1951). It is therefore a logical procedure to paralyse the respiratory muscles when indicated and to carry out artificial respiration until the effects of the disease have subsided. The problem then becomes one not dissimilar to the treatment of severe cases of poliomyelitis with combined bulbar and respiratory failure.

Prolonged artificial respiration, particularly in the acutely ill patient is, in itself, a hazardous procedure. The use of intermittent positive pressure respiration for this purpose, for patients anæsthetized with thiopentone and for those with "vasomotor reactivity" due to ganglion-blocking agents etc., by restricting venous return to the heart (Price *et alii*, 1952, 1954; Wittenberger and Sarnoff, 1950) diminishes the cardiac output, and predisposes to hypotension and peripheral circulatory failure. Both the abolition of normal coughing and the loss of humidification when tracheotomy is necessary contribute to major pulmonary collapse.

Experience gained in this hospital and other centres (Bower, 1954; Forbes, 1956) has suggested that tank respiration (positive-negative pressure) from the point of view of circulatory effects and ease of airway management is the most satisfactory of the methods at present available. The addition of the exsufflation bellows (Forbes, 1956) to the tank respirator, producing rapid expiratory flow rates, has greatly added to the ejection of pulmonary secretions, but in our experience has not always prevented major pulmonary collapse.

The introduction here (Colebatch, 1956) of a "mechanical cough machine" (Barach *et alii*, 1952, 1953, 1954; Bickerman and Itkin, 1954), exsufflation with negative pressure (E.W.N.P.), has been a great advance in both preventing and treating atelectasis. Humidification of the tracheotomized airway has been greatly helped by the use of apparatus[1] (Bower, 1954) which produces a continuous oxygen-aerosol vapour with a particle size one to three microns, achieving 100% saturation of inspired air and maximum penetration of the respiratory tract.

Of the drugs available, capable of producing skeletal muscle paralysis, none is free of producing undesirable side effects (Goodman and Gilman, 1955). There is little information on the effects of massive doses of these drugs in man. Succinylcholine ("Scoline") would appear least undesirable, but its rapid transient action makes it difficult to control for long-term use. Mephenesin ("Myanesin") in high concentrations causes intravascular hæmolysis, consequent hæmaturia and the disastrous effects of pigment depositions in the renal tubules. Gallamine triethiodide ("Flaxedil") causes sinus tachycardia. d-Tubocurarine ("Tubarine") causes paralysis of skeletal muscle and autonomic ganglia, and the release of significant amounts of histamine (Alan *et alii*, 1939; Comroe and Dripps, 1946). It is said to depress cells of the adrenal medulla, and thereby diminishes the secretion of adrenaline. It may decrease the motility and tone of smooth muscle, particularly of the gastro-intestinal tract and bladder. Clinically, therefore, one may expect such troublesome complications as hypotension, bronchospasm, retention of urine and paralytic ileus. This drug produces prolonged paralysis, and is effective by either intramuscular or intravenous injection. In this instance "Tubarine"[2] was used as the basic paralysing agent, together with supplements of succinylcholine chloride ("Scoline", Allen and Hanbury) as detailed in the following case report.

Clinical Record.

A healthy fourteen-year-old boy was admitted to Royal Perth Hospital on February 4, 1958, after he had dived into a muddy fresh-water pool, struck his head on some rocks and received a wound to the scalp. The wound was situated in the frontal region, was about two inches above the hairline and four inches in length, and exposed the frontal bone in its depth. It was sutured in the casualty department, and the patient admitted to the ward for observation. There was no history of previous immunization against tetanus.

On the following day his temperature was 102° F., the wound was tense and removal of sutures yielded pus. Subsequent culture showed abundant growth of *Bacterium coli*. *Clostridium tetani* was not looked for at that time, and subsequent treatment of the wound made culture of it unlikely. He was stated to be very apprehensive. On February 7 he complained of stiffness of the jaw, but no rigidity of other muscles was detected. The following morning there was generalized tonic rigidity, trismus and risus sardonicus. He was given 50,000 units of tetanus antitoxin intravenously and 50,000 units intramuscularly and transferred to the Shenton Park Annexe.

It was impossible, because of generalized and laryngeal muscle spasm and cyanosis, to pass a polythene tube into

[1] Equipment supplied by Mist-O-Gen Equipment Coy., 2711 Adeline Street, Oakland 7, California, U.S.A.

[2] The antihistamine antazoline ("Histostab", Boots) was used to control endogenous histamine release.

the stomach. This was therefore carried out under light "Pentothal" anæsthesia. At the same time a Hamilton Bailey metal cannula was inserted into the long saphenous vein at the medial malleolus. Over the next 24 hours tonic rigidity became more marked with head retraction, opisthotonus, and episodes of laryngeal and respiratory muscle spasm with accompanying cyanosis. He had bitten and severely lacerated his tongue during an episode of severe tonic spasm.

During the preceding 24 hours (February 9 to 10) he had been treated with a total of 775 milligrammes of chlorpromazine ("Largactil") and one gramme of pentobarbitone. Owing to the increasing frequency of spasms involving laryngeal and respiratory muscles, and the ineffective treatment with "Largactil" and pentobarbitone, it was decided to perform a tracheotomy, fully curarize him and carry out continuous tank respiration. At 10.30 a.m. on February 10, three days after the onset of trismus, under light "Pentothal" anæsthesia, the patient was intubated and tracheotomy performed. Immediately after this he was given 30 milligrammes of "Tubarine" in oil and 0·1 gramme of antazoline intramuscularly, and 30 milligrammes of aqueous "Tubarine" by intravenous injection. The patient was placed in a tank respirator. The subsequent management and progress were as follows.

Skeletal Muscle Relaxants.

Except for the initial intramuscular dose, all relaxants were given intravenously. For the first eight hours, 30 milligrammes of "Tubarine" were given every two hours. A flexible plan was then adopted, and a dosage of 30 milligrammes was given when diaphragmatic spasms interfered with tank respiration. These spasms were noted at roughly two-hourly intervals, and were usually preceded by movements of the tongue and lips, symmetrical clonic spasms of the upper limbs and then onset of ineffectual diaphragmatic movements. Such signs were used as indications of the need for further curarization.

During periods of gross sensory stimulation as occurred, for example, during sponging and chest percussion, and the use of the E.W.N.P. machine, it was sometimes found that clonic spasms interfered with the control of artificial respiration. On these occasions 100 milligrammes of "Scoline" were given intravenously, and rapid and complete relaxation was obtained, enabling treatment to proceed smoothly. Table I shows the daily and total dose of relaxants used. On the thirteenth day of tank respiration, the patient's spasms and hence "Tubarine" requirements diminished, and by the sixteenth day no further relaxant was needed. It is interesting to note this rapid fall in requirements (see Figure I).

Respirator Management.

The calculated required tidal volume (Radford *et alii*, 1954) in this patient was 300 millilitres at a rate of 16 per minute. At this volume clinical cyanosis was evident, and respirator pressures were increased to give a tidal volume of 500 millilitres, at which level the patient's colour was satisfactory. The tidal volume was measured at the tracheotomy with nose and lips closed, using a low resistance gas meter spirometer.

Oxygen was given continuously as oxygen-aerosol[1] nebulization via the tracheotomy. Frequent suction of the tracheotomy was necessary. Secretions became purulent on the sixth day of treatment, *Staphylococcus aureus* being cultured, and erythromycin was administered.

Mechanical coughing was carried out in the tank respirator (by increasing the negative pressures for eight respiratory cycles) each half hour. Three times in each day coughing was carried out with the E.W.N.P. machine after sponging. Regular X-ray examinations of the chest showed clear lung fields throughout the period of treatment.

When the tank needed to be opened for treatment, sponging, etc., respiration was continued with the Royal Melbourne Hospital Resuscitator via the tracheotomy cannula, delivering 100% oxygen to the airway at a pressure not exceeding 40 millimetres of mercury.

[1] Aerosol prescription: glycerine, two fluid ounces; propylene glycol, two fluid ounces; 1% "Neo-Synephrine", eight fluid ounces; 50% "Aviscour", six minims; water to 80 fluid ounces. Antibiotics or bronchodilators may be added to this solution.

TABLE I.

The Daily and Total Doses of "Tubarine" and "Scoline".

Day of Tank Respiration.	"Tubarine." (Milligrammes.)	"Scoline." (Milligrammes.)
1	350	—
2	330	100
3	330	100
4	300	—
5	390	—
6	330	—
7	345	—
8	285	100
9	300	100
10	360	—
11	240	—
12	285	—
13	320	—
14	195	—
15	165	100
16	—	—
17	—	—
18	—	—
Total ..	4525	500

Vomiting in the respirator is frequently a major threat to the airway. Hourly (or more frequently if indicated) routine aspiration of the stomach has been found here to be an excellent prophylaxis and a good index in detecting the onset of ileus.

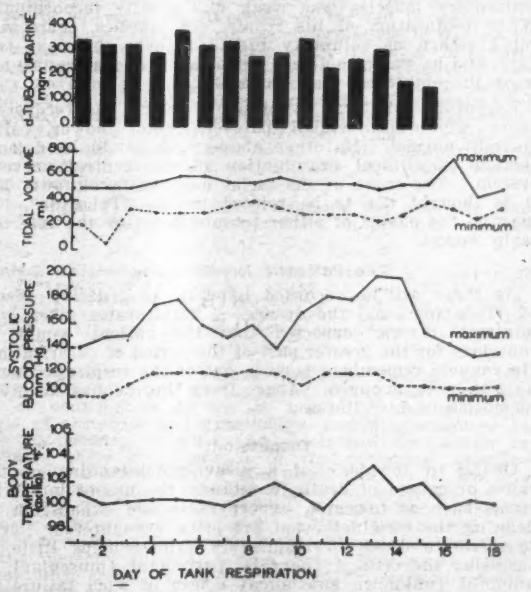

FIGURE I.

The body temperature, systolic blood pressure, tidal volume and administration of "Tubarine" during the 18 days of tank respiration.

A routine ward diet (supplemented with "Penta-vite" 0·3 millilitre three times a day) was reduced to a fluid consistency by a vitamizer and given via the tube. The patient's fluid requirements were given in between these feedings. At no time was there failure to absorb the food so given, nor was there any distension of the intestine. Defæcation took place spontaneously on the

fourteenth day. There was no retention of urine, the bladder emptying fully at regular intervals.

The patient's blood pressure was taken at frequent intervals. Hypotension was never seen. (Hypotension has been observed in two patients, aged 34 and 65 years respectively, after injection of "Tubarine". It has always been promptly restored to its original level by the use of antihistamines given intravenously.) The blood pressure was sometimes elevated (Figure I), most often coinciding with a fall in tidal volume and hence carbon dioxide retention.

Apart from the initial dose of antihistamine given at the commencement of curarization, further doses were given when there was thought to be clinical indication of excessive histamine release. For example, on the third day an urticarial rash was noted on the skin, which promptly subsided after 0·1 gramme of antazoline was given intramuscularly. Altogether, 0·4 gramme was given over the eighteen-day period in the respirator.

Phenobarbitone, 0·5 grain (32 milligrammes), was given twice a day, and pentobarbitone 1·5 grains (97 milligrammes) at night. No other sedation was used.

Return of Voluntary Muscle Power.

Complete flaccidity was present for the first 10 days. Full-range passive movements were given to all limbs each day. On the eleventh day the "Tubarine" requirements commenced to fall (Figure I); the patient was able to open his eyes and move his upper limbs on request. On the twelfth and thirteenth days "Tubarine" requirements again rose to the previous levels, and no voluntary muscle power was noted. From the thirteenth day onwards the requirements fell sharply, and by the sixteenth no further "Tubarine" was necessary. By this time full voluntary muscle power was present in all four limbs, although artificial respiration was continued, and the patient had only a few minutes of self breathing. The power of the respiratory muscles was weak and grossly incoordinate. With re-education of his respiratory muscles, there was rapid return of voluntary breathing over the next two days, and he was completely independent of respiratory aid from the eighteenth day onwards.

Except for bilateral facial palsy, which has recovered, there were no residual pareses, motor power being entirely normal. No other abnormality could be demonstrated on clinical examination of the central nervous system. The cause of the facial palsy is not known, but it is thought not to be related to the "Tubarine". It may be the effects of either tetanus toxin or the infected scalp wound.

The Patient's Recollections.

As there are no recorded hypnotic or sedative effects of "Tubarine" and the dosage of barbiturates given was minimal, it was expected that the patient would be conscious for the greater part of the period of curarization. He vaguely remembers periods out of the respirator when he was being sponged. Apart from this he has no other memories of his illness.

Discussion.

Owing to the lack of a clear understanding of the cause or causes of death in tetanus, the use of indefinite terms such as toxæmia, hyperpyrexia and exhaustion in defining the terminal event are often encountered. Even to attribute death to respiratory failure helps little in assessing the central (neural), peripheral (muscular) or humoral (unknown substance) origin of such failure. It does appear that either anoxæmia, which may be cumulative consequent upon repeated respiratory muscle spasm (Pelloja, 1951), or respiratory centre failure (due to an unknown substance liberated from toxin fixed to the anterior horn cells as suggested by Firor *et alii*, 1940) is the prime factor leading to death in the majority of cases. Accepting the primacy of the anoxæmia death hypothesis, it must be further agreed that heavy sedation, particularly with barbiturates, may worsen an already precarious state. Hence a new concept of treatment must arise, in which the aim is to provide the patient with adequate ventilation until such time as the respiratory effects of the disease have subsided or some previously hitherto unapparent effect of the toxin (Pelloja, 1951) supervenes to cause death. Our present difficulty is to detect early enough those patients in whom respiratory failure will be a major problem.

Some certainty exists in the prognosis. As regards age, the best survival is seen in the second and third decades of life (Christiansen and Thurber, 1957). An incubation period of less than nine days and a period of onset (the time between the first symptom and the first spasm) of less than 48 hours carried a mortality rate of 79% in a recent group study (Johnstone, 1958).

The modifying effects of treatment are difficult to assess. Christiansen and Thurber (1957), in a series of 91 patients collected from the Mayo Clinic, noted a fall in the mortality rate from 57% for the ten-year period 1925 to 1934 to 27% for the decade 1945 to 1954. They attributed the fall to improved therapeutic measures, e.g., the use of antibiotics.

In the case described here, after the induction of paralysis, it was found that management differed very little from that of patients severely affected with bulbospinal poliomyelitis, of which much experience has been gained at this centre. The necessity for accurate observation of spasm and thus the decision of when to give a further dose of relaxant demanded the twenty-four-hour attention of a resident medical officer. It may well be possible to overcome this aspect and at the same time achieve smoother control of spasm by making use of electromyography and by engineering a servo-mechanism to regulate the amount of relaxant needed.

In general, the method, as described in detail, proved satisfactory, and it appears a suitable one for the severe case in which it is clinically apparent that death from respiratory failure will be the outcome. The efficacy of this method needs to be tested in a large series.

Summary.

1. A case of severe tetanus with a three-day incubation period and a period of onset of 24 hours is described.

2. Basic treatment was with d-tubocurarine and tank respiration.

3. The patient survived after a period of 15 days' continuous artificial respiration, during which time 4525 milligrammes of "Tubarine" and 500 milligrammes of "Scoline" were administered. He is well.

4. Owing to the significant histamine release with d-tubocurarine, an antihistamine should be given initially as a prophylactic measure and as required from subsequent clinical observations.

5. Anoxæmia is emphasized as the commonest cause of death in tetanus.

Acknowledgements.

I wish to thank Dr. I. O. Thorburn and Dr. E. R. Beech, under whose care the patient was treated, for permission to publish this case.

References.

ALAN, M., ANREP, G. V., BARSOUM, G. S., TALAAT, M., and WIENINGER, E. (1939), "Liberation of Histamine from the Skeletal Muscle by Curare", *J. Physiol. (Lond.)*, *95*: 148.

BARACH, A. L., BECK, G. J., BICKERMAN, H. A., and SEANOR, S. E. (1952), "Physical Methods Simulating Mechanisms of the Human Cough", *J. app. Physiol.*, *5*: 85.

BARACH, A. L., BECK, G. J., and SPANIER, M. (1954), "Exsufflation with Negative Pressure: Physical and Clinical Studies in Poliomyelitis, Bronchial Asthma, Pulmonary Emphysema and Bronchitis", *Arch. intern. Med.*, *93*: 825.

BICKERMAN, H. A., and ITKIN, S. (1954), "Exsufflation with Negative Pressure (E.W.N.P.). Elimination of Radiopaque Material and Foreign Bodies from Bronchi of Anæsthetized Dogs", *Arch. intern. Med.*, *93*: 698.

BOWER, A. G., EDITOR (1954), "Diagnosis and Treatment of the Acute Phase of Poliomyelitis and its Complications", Williams and Wilkins, Baltimore.

CHRISTENSEN, N. A., and THURBER, D. L. (1957), "Clinical Experience with Tetanus: 91 Cases", *Proc. Mayo Clin.*, *32*: 146.

COLEBATCH, H. J. H. (1956), personal communication.

COMROE, J. H. junior, and DRIPPS, R. D. (1946), "The Histamine Like Action of Curare and Tubocurarine Injected Intravenously and Intra-Arterially in Man", *Anesthesiology*, 7: 260.

FIROR, W. M., LAMONT, A., and SCHUMACKER, H. B. (1940), "Studies on the Cause of Death in Tetanus", *Ann. Surg.*, 3: 246.

FORBES, J. (1956), personal communication.

GARCIA-PALMIERI, M. R., and RAMIREZ, R. (1957), "Generalized Tetanus: Analysis of 202 Cases", *Ann. intern. Med.*, 47: 721.

GOODMAN, L. S., and GILMAN, A. (1955), "The Pharmacological Basis of Therapeutics", 2nd Edition, MacMillan, New York.

JOHNSTONE, D. D. (1958), "Tetanus in Nigeria", *Brit. med. J.*, 1: 12.

PELLOJA, M. (1951), *"Le tétanos expérimental par la toxine tétanique"*, Masson, Paris.

PRICE, H. L., CONNOR, E. H., ELDER, J. D., and DRIPS, R. D. (1952), "Effect of Sodium Thiopental on Circulatory Response to Positive Pressure Inflation of the Lungs", *J. Appl. Physiol.*, 4: 629.

PRICE, H. L., CONNOR, E. H., and DRIPS, R. D. (1954), "Some Respiratory and Circulatory Effects of Mechanical Respirators", *J. Appl. Physiol.*, 6: 517.

RADFORD, E. P. junior, FERRIS, B. G. junior, and KRIETE, B. C. (1954), "Clinical Use of a Nomogram to Estimate Proper Ventilation during Artificial Respiration", *New Engl. J. Med.*, 251: 877.

WHITTENBERGER, J. L., and SARNOFF, S. J. (1950), "Physiologic Principles in the Treatment of Respiratory Failure", *Med. Clin. N. Amer.*, 34: 1335.

Reviews.

Blood Groups in Man. By R. R. Race, Ph.D., M.R.C.S., F.R.S., and Ruth Sanger, Ph.D., B.Sc.; Third Edition; 1958. Oxford: Blackwell Scientific Publications. 8½" × 5½", pp. 400. Price: 42s. (English).

THE third edition of this book has all the brilliance and verve of its predecessors. The favourable general comments made on the second edition (1954) in this Journal (May 14, 1955) are therefore still applicable.

A remarkable feature of this new edition is that the book has actually a few pages less than the previous one, although it has similar pleasing type and spacing, and in spite of the sustained and ever-growing interest in blood groups, which has resulted in a large volume of new work since 1954. In the words of the authors "something fresh has been learnt about all of them".

The prevention of increase in size, which might have seemed inevitable, has been achieved by selective condensation and pruning of the text, to which much thought has obviously been given, so that there is a smooth evolution, as it were, from the second to the third edition. Apart from occasional typographical errors, there is little to criticize and a great deal to appreciate in this book. Recent work from laboratories in many countries is discussed, and its established or potential significance evaluated with the authors' inimitable clarity and ability to convey a sense of delight and excitement over important discoveries. There is adventure in prospect, too, when they prophesy that some of the work now in progress may soon provide solutions to problems which at present seem very complex and baffling, the interrelation of the A B O groups, secretion and the Lewis groups being a notable example.

Hermaphroditism, Genital Anomalies and Related Endocrine Disorders. By Howard W. Jones, jnr., M.D., and William Wallace Scott, M.D., Ph.D.; 1958. Baltimore: The Williams and Wilkins Company. 10¼" × 7¼", pp. 482, with 466 illustrations. Price: £8 16s.

THIS outstanding new work brings together in a single volume the present knowledge on the subject of abnormalities of sexual development. Dr. Jones, a gynæcologist, and Dr. Scott, a urologist, have both had extensive experience, in that they have carried out corrective procedures and exploratory laparotomies on large numbers of patients in the clinics of the Johns Hopkins Hospital. They have worked in close association with the adult and pædiatric endocrine clinics, and consulting authors include J. E. Howard, H. F. Klinefelter and J. G. McAfee, while Professor Alfred Jost, of the University of Paris, writes on embryonic sexual differentation.

The first chapter is an interesting account of the origin of the concept of hermaphroditism in Græco-Roman culture, and this is followed by chapters on the criteria of sex and the principles of treatment. The next section deals with intersexuality, with gonadal insufficiency, Klinefelter's syndrome and true hermaphroditism. Then follow long chapters on male and female hermaphroditism with and without adrenal hyperplasia, and then shorter chapters on surgical treatment.

An excellent chapter on cryptorchidism presents the mechanism of descent, complications and treatment. The author (Dr. Scott) states that late spontaneous bilateral descent will take place at puberty in 69% of cases, and that interference before then is not advised. He does not favour hormonal therapy, and believes that anatomical and mechanical causes are the basis for nearly all failures of descent at puberty. In these cases surgical exploration should be undertaken.

The chapter on hypospadias is outstanding and is well worth perusal by all urologists. The Cecil procedure is preferred to be carried out in two stages before the child reaches school age. Burying the penis in the scrotum gives a lower incidence of fistula than the Denis Browne technique. At least two months should be allowed between the stages, and perineal drainage is used. Tumours of the ovary and testis are then considered, and finally 70 pages are devoted to the adrenals and their surgery.

This work is a magnificent achievement, lavishly illustrated on high-class paper, very readable and the result of much research. It must be considered the outstanding work on this subject, and an essential book of reference for every gynæcologist and urologist.

Dukes' Bacteria in Relation to Nursing. Revised by Stanley Marshall, M.D., B.S., M.R.C.S.; 1958. London: H. K. Lewis and Company, Limited. 8½" × 5½", pp. 224, with 18 illustrations. Price: £1 1s. (English).

THIS book, as is stated in the preface, is intended to be an introduction to bacteriology for tutor sisters and nursing staff. It provides such a complete survey of the subject, in admirably lucid terms, that its usefulness may extend beyond the purpose for which it was written. Medical officers, as well as senior sisters, could well use this book for reference when preparing to lecture to nurses.

Systematic and practical bacteriology is covered surprisingly well for a book of this size. This information would be of value for reference or for aid in setting up demonstrations, rather than as information to be learnt by examinees on the nursing staff. It is a little disappointing, since such great advances in diagnostic virology have been made, that the new chapter on viruses does not deal with the subject more fully. The sections on immunity, collection of specimens, sterilization, cross-infection and antibiotics are all excellent. The chapters on antiseptics and disinfectants would need amplification to cover some of the newer preparations in common use in Australian hospitals.

The printing is excellent, illustrations are adequate, and this book maintains the standard set in previous editions.

***Clinical Obstetrics and Gynecology*: Volume I, Number 2:** "Toxemias of Pregnancy", edited by Louis M. Hellman, M.D.; "Fibromyomas of the Uterus", edited by Robert A. Kimbrough, M.D.; 1958. New York: Paul B. Hoeber, Inc. 9½" × 6½", pp. 256, with many illustrations. Price not stated.

THE papers in the second quarterly number of this series, 24 in number, are again of a high standard. The list of contributors is one of household names in the world of obstetrics and gynæcology. Following chapters on the biochemistry of fluid and electrolyte metabolism in toxæmia, there are accounts of the peripheral vascular bed and the circulation of the brain with J. C. McClure Browne contributing that on the uterine circulation in toxæmia. The pathology of the placenta and endocrine aspects of toxæmia are included. R. H. J. Hamlin has been invited to write on the results of the anti-toxæmia campaign at the Women's Hospital, Crown Street, Sydney—an article which must create an impression in many overseas schools. Professor Assali's practical paper on the treatment of pre-eclampsia and eclampsia emphasizes the decreasing use of cerebral depressants like morphine, and the increasing use of the vasodepressor drugs—reserpine, veratrum and "Apresoline". Professor Sheehan of Liverpool writes an excellent chapter on the causes of maternal death, describing the pathological findings associated with each mode of death.

Easier to read and full of interest, yet no less informative, is the symposium on fibromyomata. Discussing symptoms and signs, Daniel G. Morton makes the point that except for submucous pedunculated tumours, fibroid tumours are associated with hæmorrhage more than the cause of it. They tend to prolong the menstrual life, and 95% of women menstruating at the age of 53 years have fibroids.

Edmund Novak writes on benign and malignant changes in fibroids, Houston Everett on the effect of myomata on the urinary tract, and Rubin on their association with sterility.

Kimbrough, discussing methods of treatment, makes a plea for the conservation of the ovaries before the age of 55 years. He reminds us that post-menopausal enlargement of fibroids may be due to benign as well as to malignant degeneration.

Eugene A. Edwards and Robert A. Beebe give the indications and contraindications for vaginal hysterectomy, this being the operation of choice for the treatment of fibroids up to the size of a three and a half months' pregnancy. The technique of morcellation is illustrated.

Counsellor and Welsh, of the Mayo Clinic, give a splendid description of vaginal hysterectomy for fibroids, also illustrating morcellation and hemisection of the uterus.

Te Linde's chapter on abdominal hysterectomy, as would be expected, contains much good advice. His discussion of the pros and cons of total and subtotal hysterectomy is excellent. He condemns the widespread practice of operating on a patient just because the cervix "looks bad".

As with the first number in this series, the book is a delight to read and study. The symposium on fibromyomata should be read by all who operate on the female pelvis.

The Long Road Back: The Story of My Encounter with Polio. By Edward Le Comte; 1958. London: Victor Gollancz, Limited. 7¾" × 4¾", pp. 192. Price: 20s. 6d.

THIS book deals with the author's contraction of poliomyelitis whilst touring the Continent on leave of absence from Columbia University. It depicts his triumph over his disability and his rehabilitation to useful citizenship as a lecturer in English literature at his former university. For the average reader the story is dragged on through numerous minor experiences, with the introduction of many not very interesting characters, and would prove heavy going. For the person who has experienced poliomyelitis it is but a repetition of his own ordeal told without much humour. For the doctors, physiotherapists, nurses and others concerned with the treatment of these patients, it presents many aspects relating to the patient's physical well-being which a number of the profession could learn with profit. This knowledge would make the painful acute stage of this complaint much easier for the patient to bear. In his references to "no disease being more painful than this one in its acute phase", to the difficulties and physical adjustments necessary to obtain sleep and to the varying opinions existing amongst the medical profession on how to handle these patients, and later in his reference to the remarkable fatigue experienced when attemping the most minor form of activity and the fears existing when eventually the first tentative efforts towards normal living are made, the author has given a true and realistic insight into the feelings and difficulties of these patients. In all, the medical profession does not emerge with credit.

The story could have been more briefly and brightly told, but despite its shortcomings should be read by all who claim to treat poliomyelitis.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Pediatric Methods and Standards", edited by Fred H. Harvie, M.D.; Third Edition; 1958. Philadelphia: Lea and Febiger; Sydney: Angus and Robertson, Limited. 8" × 4¾", pp. 330, with many tables. Price: 49s. 6d.

"The primary purpose of the book is to serve as a pocket memory for factual data and test methods, with enough text to facilitate their usage."

"Fragilitas Ossium Hereditaria Tarda: Ekman-Lobstein Disease", by Angelo Caniggia, Carlo Stuart and Renza Guideri; *Acta Medica Scandinavica*, Supplementum 340; 1958. 9¾" × 6¾", pp. 172, with 73 illustrations. Price not stated.

The authors are from the University of Sienna, Italy.

"The Significance of Hæmorrhage during Treatment of Patients with the Coumarin Anticoagulants", by M. A. Peyman; *Acta Medica Scandinavica*, Supplementum 339; 1958. 9¾" × 6¾", pp. 64, with 16 tables.

The author is from Charing Cross Hospital, London.

"Re-Education of the Injured Shoulder", by R. Barrie Brookes, F.C.S.P.; 1959. Edinburgh and London: E. and S. Livingstone, Limited. 8¾" × 5¼", pp. 120, with 59 illustrations. Price: 12s. 6d. (English).

Based on extensive experience at the Birmingham Accident Hospital.

"Manual of Chest Clinic Practice in Tropical and Sub-Tropical Countries", by A. J. Benatt, M.D.; 1959. Edinburgh and London: E. and S. Livingstone, Limited. 7¼" × 4¼", pp. 108, with illustrations. Price: 10s. 6d. (English).

The author was formerly Senior Adviser to the World Health Organization.

"*A Concise Textbook of Anatomy and Physiology*: Applied for Orthopædic Nurses", by Joyce W. Rowe, S.R.N., S.C.M., O.N.C., and Victor H. Wheble, M.A., B.M., B.Ch. (Oxon.), F.R.C.S. (Ed.), Dip. Méd. Col. (Antwerp); 1959. Edinburgh and London: E. and S. Livingstone, Limited. 8¾" × 5¼", pp. 692, with 332 illustrations. Price: 35s. (English).

Primarily for orthopædic student nurses, it may also be of value to students of occupational therapy, physiotherapy, remedial gymnastics and radiography.

"A Laboratory Manual on Abnormal Hæmoglobins", prepared under the direction of J. H. P. Jonxis and T. H. J. Huisman; 1958. Oxford: Blackwell Scientific Publications. 8¾" × 5¼", pp. 44, with 12 illustrations and two tables. Price: 9s. 6d. (English).

Prepared for the Council for International Organizations of Medical Sciences and the Middle East Science Co-operation Office of UNESCO.

"Recent Studies in Epidemiology", edited by J. Pemberton, M.D., M.R.C.P., D.P.H., and H. Willard, M.D.; 1958. Oxford: Blackwell Scientific Publications. 8¾" × 5¼", pp. 220, with many illustrations. Price: 25s. (English).

Papers presented at the Study Group on Current Epidemiological Research organized by the International Corresponding Club (Preventive and Social Medicine) at Noorwijk aan Zee, Holland, in September, 1957.

"Symposium on Rheumatoid Arthritis: Differential Diagnosis and Treatment", edited by Nanna Svartz and Börje Olhagen; *Acta Medica Scandinavica*, Supplementum 341, accompanies Volume 162, 1958. 9¾" × 6¾", pp. 262, with many illustrations.

The record of a symposium held in Stockholm in April, 1957.

"Science News", edited by Archie and Nan Clow, Number 50, 1958. Mitcham, Victoria: Penguin Books Proprietary, Limited. 7" × 4", with illustrations. Price: 4s.

Six articles on various aspects of science, including one on the voyages of H.M.S. *Beagle*, with the usual research report and book reviews.

"Clinical Obstetrics and Gynecology", Volume I, Number 4; December, 1958. Symposium on Operative Obstetrics", edited by J. Robert Willson, M.D.; "Symposium on Genital Cancer", edited by Daniel G. Morton, M.D. New York: Paul B. Hoeber, Incorporated. 9¾" × 6¾", pp. 281, with illustrations. Price: $18 per year (four issues).

The latest volume of a useful new quarterly publication.

"Rehabilitation of the Hand", by C. B. Wynn Parry, M.B.E., M.A., D.M., D.Phys.Med., assisted by N. R. Smythe, M.A.O.T., and L. E. Baker, M.C.S.P.; 1958. London: Butterworth and Company (Publishers), Limited. 9¾" × 6¾", pp. 292, with 101 illustrations. Price: 63s. 6d. (English).

The book attempts to provide full details of methods in the rehabilitation of the hand.

"Diseases of Women", by Ten Teachers, under the direction of Frederick W. Roques, C.B.E., M.D., M.Chir., F.R.C.S., F.R.C.O.G., edited by Frederick W. Roques, John Beattie and Joseph Wrigley; Tenth Edition; 1959. London: Edward Arnold (Publishers), Limited. 8¾" × 5¼", pp. 576, with 209 illustrations. Price: 36s. (English).

This well-known book, first published in 1919, has been fully revised.

"Clinical Neurosurgery: Proceedings of the Congress of Neurological Surgeons, Washington, D.C., 1957"; Volume V. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" × 5¾", pp. 226, with many illustrations. Price: 38s.

Most of the papers are devoted to the problems of neurological surgery in childhood.

The Medical Journal of Australia

SATURDAY, APRIL 11, 1959.

THE TREATMENT OF TETANUS.

WE have recently discussed the prevention of tetanus in these columns. A report of a case by Gordon Sarfaty published elsewhere in this issue (page 496) may serve as a text for some remarks on the treatment of tetanus. Perhaps we should begin by congratulating Sarfaty on the successful outcome of a case in which the prognosis at the onset was, by all accepted criteria, very bad. Several reports of successful treatment in similar desperate cases have now been published, and it seems quite clear that in such cases it is necessary to mobilize the full resources of a centre with the best modern equipment, and preferably a team familiar with this type of case. It is no accident that recent advances in the treatment of tetanus owe much to those who have had special experience in the treatment of bulbar poliomyelitis.

There is still a considerable divergence of views on many aspects of the treatment of severe tetanus. There is no agreement on how far sedation can be carried and when complete curarization is called for. The claims for the advantages of chlorpromazine as against barbiturates are by no means generally accepted. It is undecided whether such a patient should be fed by stomach tube or intravenously. If curarization is decided on, what is the best type of respirator? The answer to this will depend to some extent on local availability and experience. Some authors have even questioned the value of anti-tetanus serum in the treatment of established tetanus.

As Sarfaty points out, since death in cases of severe tetanus is frequently due to respiratory failure, in such cases it seems a logical procedure to treat the patient by paralysing the respiratory muscles and maintaining respiration by artificial means. However, the problems involved in keeping a patient alive for two or three weeks under such conditions are formidable, and the first reports of the success of this form of treatment appeared only in 1954. It would be generally agreed that resort to such a drastic form of treatment is justifiable only when the spasms and respiratory difficulty cannot be controlled by sedation, but there is difference of opinion as to how far sedation can be carried. R. S. Packard and his colleagues[1] at the Royal Prince Alfred Hospital, Sydney, have described the successful treatment of two patients with severe tetanus by heavy sedation with chlorpromazine combined with moderate doses of amylobarbitone, without the use of relaxants; in both cases the patient's caloric, protein and fluid requirements were administered entirely by vein during the critical period of the illness—in one case this was maintained for over a fortnight. Intravenous feeding eliminated one serious danger in such patients, that of inhalation of regurgitated stomach contents. In their comments Packard and his colleagues imply that a large proportion of cases, even of severe tetanus, should be amenable to their regimen, which is based primarily on the use of a very heavy dosage of chlorpromazine. On the other hand, in Sarfaty's case the patient had failed to respond to a dosage of chlorpromazine fully comparable with the amounts used by Packard when the decision was made to resort to complete curarization and artificial respiration. There is clearly a place for both types of treatment in the appropriate circumstances. Recent reports from England suggest the widespread adoption there of complete curarization and artificial respiration in the treatment of severe tetanus, but some of these reports refer only to barbiturates as the means of sedation. Chlorpromazine in really adequate doses has been advocated in several recent papers as possessing special advantages in the treatment of tetanus, with the statement that in some earlier reports in which the value of chlorpromazine had been doubted, conclusions were based on cases in which the dosage used was quite inadequate.

In a recent paper from South Africa, D. R. Laurence *et alii*[2] report the results of a trial in which chlorpromazine was compared with barbiturates in the treatment of 75 tetanus patients; they found no appreciable difference between the results obtained with these drugs. However, 31 of these patients were neonates, of whom 25 died; of the remaining 44 patients, 21 died, and a study of this paper by Laurence *et alii* suggests that under the conditions of their trial (i.e. with the resources available to them) a large proportion of patients with really severe tetanus died whichever drug was used, and that this trial was therefore not a fair test of the value of chlorpromazine in critical cases in which more intensive therapy was possible. Certainly a number of other reports suggest that chlorpromazine supported by moderate doses of barbiturates has very important advantages over barbiturates alone in the management of tetanus. A study of recent reports provides good grounds for the belief that important advances are being made in the treatment of severe tetanus, but that it is too soon to expect statistical evidence of the results of these advances, thus to some extent invalidating the conclusion of the report of O. Creech, A. Glover and A. Oschner[3] on the evaluation of the treatment of tetanus at the Charity Hospital in New Orleans. These authors have analyzed 558 cases of tetanus in patients admitted to that hospital between January, 1943, and September, 1956, and compared the results with those previously reported. Their paper contains much interesting information, but their final conclusion is that the decline in mortality during the period under review is but the continuation of a trend that has been going on since the beginning of the century, and is due to improved management in general rather than to any single factor in treatment. While it is still true that the management of severe tetanus has many facets, all of which may be vitally important, it is possible that the stage is now set for a really significant decline in the mortality from this dread disease.

[1] *Brit. med. J.*, 1958, 1:16 (January 4).

[1] *Lancet*, 1958, 1:987 (May 10).

[2] *Ann. Surg.*, 1957, 146:369 (September).

This raises the question of where cases of severe tetanus should be managed. Sarfaty remarks of his own case that "after the induction of paralysis, it was found that management differed very little from that of patients severely affected with bulbous spinal poliomyelitis, of which much experience has been gained at this centre". This statement illustrates plainly the advantage of treating tetanus in specially equipped units. This question was recently posed in our correspondence columns,[1] and it is one which deserves serious consideration. Patients with even moderately severe tetanus can be, and are, successfully treated at country hospitals; but in the most severe cases, the advantages of a specially equipped centre, where it is possible to have a doctor in attendance 24 hours a day, with nursing staff experienced in the specialized procedures involved, physiotherapists to supervize postural drainage at frequent intervals, bronchoscopy as required, and the resources of a laboratory equipped to study the patient's electrolytes—these must surely tell in the patient's favour. How is one to know at the onset whether any particular patient will get by with adequate sedation and good nursing, or will need the utmost in therapeutic resourcefulness? Should all patients with tetanus be transferred to special centres as soon as the diagnosis is made? Is this practicable? At a meeting of the Royal Society of Medicine, A. Crampton Smith is reported[2] as saying that at Oxford a patient with tetanus is first anæsthetized, then paralyzed, an endotracheal tube is passed, and respiration is continued manually till the patient reaches hospital, where tracheotomy is performed. This suggests that it should be possible to transport a patient by air from most places in Australia to one of the larger centres. It may be recalled that one of the patients of Packard *et alii* was taken by ambulance 280 miles from Tamworth to Sydney with a tracheotomy tube in position. This came out *en route*, illustrating the fact that the difficulties and dangers of transporting such patients are real. Do the advantages to be gained justify the risk? Even in the best hands generalized tetanus still carries a considerable mortality. The answers to these questions are not simple.

Current Comment.

INFECTIOUS MONONUCLEOSIS.

THE most curious feature of infectious mononucleosis (glandular fever) is perhaps that, in these days when the isolation of new viruses is an everyday event, its causation is still quite obscure. It is in other respects, too, an elusive disease. It must be considered in the diagnosis of any obscure case of fever or glandular enlargement. It is a disease which is considered very much more often than it is diagnosed, and the diagnosis is made tentatively very much more often than it is proved. It is probably very much commoner than is often supposed.[3] In a recent paper by two American workers, W. R. Mason, junior, and Elizabeth K. Adams,[4] the authors analyse 100 cases occurring among college students. They first discuss the question of diagnosis, pointing out that the criteria accepted for the diagnosis of infectious mononucleosis are far from uniform; as a result, in some series described other disease conditions are included, while if the criteria applied are over-strict, cases which are almost certainly ones of infectious mononucleosis are excluded. In particular, the heterophile (Paul-Bunnell) agglutination test is an uncertain aid, to which a varying degree of importance is attached by different authors. Mason and Adams point out that the test is non-specific, and that results may be influenced by variations in technique and by inherent sources of experimental error. They accept a "positive" result to this test at a titre of 1:112 or higher, combined with compatible clinical findings and a characteristic blood picture, as evidence for a definite diagnosis of infectious mononucleosis, and compatible clinical findings with either a characteristic blood picture or a "positive" result to the heterophile test as evidence for a presumptive diagnosis. Eighty-three of their cases come into the first category and 17 into the second.

Their discussion of the clinical and hæmatological aspects of the disease, in considerable detail, covers fairly familiar ground in a lucid and informative manner. One aspect of the disease which has been stressed in more recent accounts of the disease is the question of liver damage. Mason and Adams point out that pathological studies by various authors have verified the existence of hepatitis in a large majority of cases of infectious mononucleosis, but that, while some regard this as similar to the condition seen in infectious hepatitis, others find evidence of considerably less liver damage in the hepatitis of infectious mononucleosis. Mason and Adams performed liver function tests on 62 of their patients, and found that the bromsulphthalein and cephalin flocculation tests gave positive results in about three-quarters of the patients tested, but that in only a small proportion did the thymol turbidity and serum bilirubin tests give positive results. None of their patients were jaundiced, in contrast to the findings of some authors who have reported an incidence of 10% to 20% of jaundice among their patients.

As regards treatment, Mason and Adams state that in the last few years there have been several reports of favourable effects from the use of adrenal corticosteroids. They treated 17 of their patients, mainly those with the more severe symptoms, with prednisone given orally and found the results distinctly encouraging. They gave a very short course of 20 mg. of prednisone daily for from one to three days, which was then tapered off by a reduction of 5 mg. each day. Antibiotics were given concurrently as a prophylactive measure against secondary bacterial invasion. In nearly every case the patients experienced subjective relief within 24 hours, and objective improvement in the degree of pharyngitis and the size of the cervical glands was noticeable in two or three days. They found no evidence of any ill effects after the use of these doses of steroid, which did not obscure the laboratory tests. They consider that steroid therapy deserves further trial, though they admit that it remains to be shown whether it has any effect in shortening the course of the illness or in preventing complications.

LETHAL WHOLE BODY IRRADIATION.

AT the end of last year six Yugoslavs were accidentally subjected to whole body irradiation as the result of a nuclear reactor accident at the Boris Kidric Nuclear Energy Institute at Vinca near Belgrade. From physical measurements and indirectly from hæmatological examinations five of the Yugoslavs were estimated to have received near lethal doses. They were taken for treatment to Paris, where Dr. Georges Mathé of the Hôpital Hérold is known to have a bank of embryonic myeloid cells. It is for such an occasion that much radiological research effort over the last few years has been expended.

Briefly, recovery from the hæmatopoietic and lymphopoietic destruction brought about by whole body irradiation in the range varying from 500 to 1000 rads in mice, dogs, monkeys and rats has been successful when auto-

[1] MED. J. AUST., 1958, 2:463 (October 4).
[2] *Lancet*, 1958, 2:116 (May 24).
[3] MED. J. AUST., 1957, 2:27 (July 6).
[4] *Amer. J. med. Sci.*, 1958, 236:447 (October).

logous or isologous hæmatopoietic tissue has been given intravenously after irradiation. The injected myeloid cells occupy the bone marrow spaces of the animal whose own bone marrow has been destroyed by radiation and there actively multiply until they are able to supply the needs of the host. These animals have continued to do well apart from the increased aging effect brought about by radiation and the concomitant increased cancer incidence in younger age groups. In contradistinction, hæmatopoietic homografting of foreign cells, although it gives initial recovery from the acute effects of lethal whole body irradiation, is usually followed by death some months later due to the immunological incompatibility of host and donor.[1] Animals which survive by virtue of this bone marrow graft exhibit limited recolonization of lymphoid tissue; so that, although the homologous chimæra is not entirely immunologically neutral, to say the least its immunological responses are impaired. They are very prone to infection. In mice the incompatibility has been shown to be in the direction of grafted cells against the antigens of the host, and the immunological turmoil is manifested in this mammal by diarrhœa and progressive wasting leading to death. This immunological disease, or secondary radiation disease, as it is called, has not yet been observed in man. It is hoped that it may be avoided,[2] now that homologous marrow treatment is being envisaged, by invoking the principle of actively acquired tolerance in the utilization of embryonic hæmatopoietic homografts. Billingham defined actively acquired tolerance as representing "the specific and systemic failure of the mechanism of immunological response which is brought about by exposing embryos and very young animals to antigenic stimuli". The principle is used in reverse in radiation chimærism by introducing these immunologically null embryonic cells into a lethally irradiated host. This host having received probably permanent depression of its immune powers cannot in turn reject these donor cells. The donor cells tolerate the host, and immunological secondary disease is avoided. In some strains of mice the state of "tolerance" extends even a day or two into neonatal life. It would be as well to know the duration of tolerance in human embryos. A guess might be that embryonic tissue older than 32 weeks would not succeed in avoiding secondary disease. Other obstacles confronting the application of human homografting were discussed in an editorial in this journal on November 1, 1958.

The principles of isologous hæmatopoietic grafting have been applied by N. B. Kurnick *et alii*[3] recently in human beings by means of hæmatopoietic autografts. They state that because of the severe hæmatopoietic depression which results from rapid, intensive irradiation of the thoraco-lumbar region, potentially curable malignant conditions are often inadequately irradiated, and they suggest that the likelihood of salvaging such potentially curable patients would be considerably enhanced if irradiation could be pursued with less concern for the ensuing hæmatopoietic depression. Bone marrow has been collected from the sternum and iliac crests and freeze-stored according to an adaptation of the Polge-Smith-Parkes technique (Barnes and Loutit[4]). The stored marrow has then been thawed and reinjected after intensive radiotherapy, which could have been expected to produce grave marrow ablation, with consequent improvement in the marrow picture. Kurnick and his colleagues consider the procedure worthy of further trial. On the other hand, hæmatopoietic homografting has been attempted by J. W. Ferrebee and E. D. Thomas in the treatment of leukæmia.[5] Nevertheless, although it is a most interesting and very readable review of the subject, this article has not got down to marrow replacement in the treatment of leukæmic patients in the sense that the replacement of hæmatopoietic tissue was to be complete. Ferrebee and Thomas would be the first to confirm this, but they believe that steps are being taken along the right road. Indeed, the cases in which treatment was given with whole body radiation did not approach the lethal range of radiation at which wholesale destruction of bone marrow as well as of leukæmic cells, the object of the treatment, would occur. Therefore, as the immune power of the host returned after its radiation depression, the foreign graft was eliminated, and the hosts's own myeloid cells, including the leukæmic cells, again took control.

It is theoretically possible to obtain recovery from lethal whole body radiation by grafting with foreign embryonic hæmatopoietic cells, and the clinician is rightly craning over the shoulder of the investigator in this important field. To apply these findings to the treatment of leukæmia, murine or otherwise, is reckoning without the leukæmic state itself. In the Harwell Laboratory radiation doses have sometimes been used in the treatment of murine leukæmia in the supra-lethal range, where recovery from the effects of whole body radiation cannot be effected with hæmatopoietic homografts owing to the destruction of other systems (e.g. the alimentary canal). Viable leukæmic cells have still been obtained from the tissues of animals so treated. The greater wonder remains the leukæmia, and lack of further knowledge of the leukæmic cell itself is still the main stumbling block to treatment.

[1] *J. nat. Cancer Inst.*, 1958, 20: 1051.
[2] *Nature*, 1958, 181: 488.
[3] *Ann. intern. Med.*, 1958, 49: 973 (November).
[4] *J. nat. Cancer Inst.*, 1955, 15: 901.
[5] *Ann. intern. Med.*, 1958, 49: 987 (November).

THE DANGER OF STEROID-CONTAINING EYE DROPS.

In our correspondence columns this week we publish a letter (page 510) pleading for caution in the use of steroid-containing eye drops in cases of corneal ulceration. This danger is well known to ophthalmologists, as our correspondent states, but is one which needs to be widely publicized, as the penalty of ignorance in this matter is severe. The subject is dealt with more fully in a recent short article by D. P. Tucker[1]. He states that herpes-simplex keratitis is considered to be the most important corneal disease leading to loss of vision in the United States today. The herpes virus is insensitive to any known antibiotic, and there is ample evidence that adrenal steroids have a detrimental effect on the progress of the disease. The great danger lies in the fact that the disease may progress in spite of symptomatic relief owing to the anti-inflammatory effect of the steroids. Tucker points out that, without the aid of the slit-lamp microscope, the diagnosis of dendritic keratitis can easily be missed. He goes on to say:

> The red, irritated eye is diagnosed as "conjunctivitis", and one of the antibiotic-steroid combinations so widely advertised in the journals may be unwisely employed. A week or two later the patient may have a deep stromal ulcer. Under continued steroids, corneal necrosis and perforation can occur. The patient is often referred to an oculist when corneal involvement becomes grossly apparent. But even arrest of the disease at this point may leave permanent scarring in the pupillary area, and resultant visual loss.

Another American who has written extensively on the dangers of the use of steroids in herpetic keratitis is P. Thygeson of San Francisco. He considers that in America there has been an increase in the severity and frequency of the deep forms of herpetic keratitis since the advent of steroids for topical application. In one of his papers[2] he states: "In . . . our present series of 200 cases [of herpetic keratitis] we noted that the worst cases had all received cortisone or other steroids, some for prolonged periods." In some of his cases herpetic keratitis had developed while steroids were being administered for some other complaint.

Tucker also notes recent reports of fungous keratitis folowing the topical application of steroids to the eye. He concludes with the statement: "It should be apparent that physicians unskilled in ophthalmic diagnosis should never employ eye drops containing steroids when the specific diagnosis is at all uncertain."

[1] *New Engl. J. Med.*, 1958, 258: 946 (May 8).
[2] *A.M.A. Arch. Ophthal.*, 1956, 56: 375 (September).

Abstracts from Medical Literature.

OPHTHALMOLOGY.

Radioactive Isotopes.

J. W. Bettman (*A.M.A. Arch. Ophthal.*, June, 1958), discusses the uses of radioisotopes in ophthalmology. In diagnosis of malignant melanomata P^{32} has been used but because of its limitations its use is not to be regarded as a substitute for clinical acumen. Where the use of P^{32} and clinical judgement conflict then the latter should be relied upon. As regards therapy, the most important are the Sr^{90} applicator for external therapy and radon seeds for retinoblastoma. Even though Sr^{90} emits beta rays, which have a superficial effect, delayed effects of the radiation do occur. In regard to the use of radon seeds in the treatment of retinoblastoma, the author is of the opinion that radiation is better administered by the linear accelerator or by the technique of Reese. The author concludes that radioisotopes may become useful in the elucidation of physiological and pharmacological problems in the eye.

Slit Lamp Examination of the Fundus.

D. K. Pischell (*A.M.A. Arch. Ophthal.*, November, 1958), discusses the value of slit lamp examination of the fundus and the methods available to make such examination. He states that slit lamp examination of the fundus is of value in the early diagnosis of papilloedema, œdema of the macula is easily recognized and minute cysts can be seen. Larger cysts can be differentiated from holes at the macula. The exact depth of exudates and hæmorrhages can be determined. The vitreous can be examined. Very flat detachments are readily discovered. The most important help which this examination can give is in the differentiation of simple detachment from that caused by choroidal tumour or malignant melanoma.

Diabetic Retinopathy and Vitamin B_{12}.

A. J. Cameron and G. J. Ahern (*Brit. J. Ophthal.*, November, 1958), report on the treatment of diabetic retinopathy with cyanacobalamin (vitamin B_{12}). They state that cyanacobalamin was given intramuscularly daily for 14 days in doses of 1000 microgrammes to ten selected patients. Of these ten patients, five had improved. In three cases the degree of exudate in the retina had decreased. No lessening of exudate was noted in the control subjects.

Penetrating Keratoplasty.

B. D. Leahey (*Amer. J. Ophthal.*, October, 1958), discusses his experiences in 148 cases of keratoplasty. Unfavourable cases are those in which there is dense scarring of the entire cornea, vascularized pannus from old trachoma or severe chemical burns and œdema of the cornea as in Fuchs's dystrophy. Most favourable cases are small central scars, keratoconus, Groenouw's dystrophy and lattice keratitis, diffuse thin scarring from phlyctenular keratitis and old interstitial keratitis. Many eyes, otherwise hopelessly scarred, can be made suitable for grafting by destroying blood vessels, by diathermy, peritomy and radiation. The author favours a 5 mm. graft from a donor eye not more than 20 hours old. The 5 mm. graft is fixed with two or four direct sutures and overlapping stitches. In grafts of 7 mm. or more, 10 to 20 direct sutures are used. At the end of the operation air is injected into the anterior chamber. Complications encountered are dislocation of the graft, anterior synechiæ, glaucoma, injury to the lens, vascularization of the graft, proliferation of tissue on the posterior surface of the graft, œdema of the graft, infection and recurrence of the original pathological condition.

Tonography and Angle-Closure Glaucoma.

B. Becker and H. Thompson (*Amer. J. Ophthal.*, September, 1958), have investigated the mydriasis provocative test and tonography as a means of diagnosing angle closure glaucoma and also the use of tonography as a guide to the type of surgery indicated. Of 58 normotensive eyes with narrow angles subjected to the mydriasis provocative test, 28% were found to have a rise in intraocular pressure of 8 mm. of mercury, or more. However, in 67% a decrease in outflow facility of more than 25% was demonstrated. Of the 58 eyes, 32 presented reasonable clinical evidence of being capable of angle closure. In studying therapy, 209 operations were performed on 182 eyes. Only 9% of eyes with angle closure glaucoma failed to be controlled by surgical or medical means. In discussing diagnosis, the authors make the point that in eyes with clinical evidence of angle closure a significant rise in pressure after instillation of a mydriatic occurred in less than 50%. They consider that all patients whose eyes present a gonioscopic picture of narrow angles should be subjected to the mydriasis test combined with tonography. In discussing therapy they state that a pre-operative outflow facility value greater than 0·15 is adequate for pressure control and in these eyes a simple peripheral iridectomy will suffice. On the other hand eyes with a facility of outflow of 0·10 or less are best treated by iridencleisis as an initial procedure. Where outflow facility value is between 0·10 and 0·15 the authors recommend peripheral iridectomy, and if this fails that it should be followed by iridencleisis.

Lens Induced Uveitis and Glaucoma.

P. A. Chandler (*A.M.A. Arch. Ophthal.*, November, 1958), draws attention to uveitis and glaucoma due to lens reaction. He states that the important thing is to recognize that the lens or residual lens matter is the cause of the inflammation, and that the removal of the lens or the residual lens matter is the most important factor in the relief of the trouble. He reports on eleven cases to illustrate various aspects of lens induced uveitis. In glaucoma and uveitis due to hypermature cataract the treatment is removal of the lens even though light projection is faulty, as poor light projection is not unusual in these cases and in most cases return of function after operation is usual. After extracapsular extraction with retained cortex there may be minimal reaction, and complete absorption with good function. In these people there is no sensitivity to lens protein. In others the post-operative course is stormy, and in these there is considerable residual cortex and a sensitivity to lens protein. Medical treatment may produce some improvement but inflammation never ceases until all residual lens matter is absorbed or removed. Operation for the removal of the residual lens matter to which the patient is sensitive should be performed within a few weeks of the lens extraction. Removal of lens matter even months after the extraction will result in a white eye, but the eye will not regain normal function. It is better to remove the offending lens or residual lens matter than to remove the eye.

Steroid Therapy and Intraocular Pressure.

Pei-Fei Lee (*Amer. J. Ophthal.*, September, 1958), has studied the influence of systemic steroid therapy on the intraocular pressure in 13 patients with severe asthma who were under steroid therapy for a long period of time, but who otherwise were normal. He studied intraocular pressure, facility of outflow and the gonioscopic appearances. It was found that there was no significant tendency to elevation of intraocular pressure or impaired facility of outflow in this group.

Intravenous Sedation in Cataract Surgery.

C. D. Townes and S. H. Mann (*Amer. J. Ophthal.*, August, 1958), outline their anæsthetic technique in cataract surgery. The evening before operation the patient is given 1·5 grains of "Seconal" and this dose is repeated two hours before operation. One hour before operation 50 or 75 mg. of pethidine are given. In the theatre a mixture containing chlorpromazine, 25 mg., promethazine, 50 mg., pethidine, 100 mg, and saline, 25 ml., is given intravenously at the rate of 1 ml. per minute until the patient is asleep; 7 ml. was found to be the average dose. Five minutes later the usual injections for anæsthesia and akinesia are given, and pressure over the globe is then applied for five minutes. Oxygen at the rate of one litre per minute is administered under the drapes. The only side effect was a fall in blood pressure and this could be overcome by the intramuscular injection of 0·2 ml. of "Neosynephrine".

OTO-RHINO-LARYNGOLOGY.

Ménière's Disease Treated with Ultrasonic Waves.

F. Altmann and J. G. Walner (*A.M.A. Arch. Otolaryng.*, January, 1959), discuss the treatment of Ménière's disease with ultrasonic waves. They state that medical treatment of this condition has remained far from satisfactory and that surgical destruction is of limited application. A new method aimed at selective destruction of the disused vestibular portion of the labyrinth with

ultrasonic waves whilst preserving the cochlear portion would be ideal for the treatment of ears which do not respond to medical treatment and which are unsuitable for surgery. The authors then review some of the early work and the more recent work of Arslan of Padua. Arslan uses a thin and narrow sound wave emitter producing a narrow beam of sound waves with a frequency between 800,000 and 1,000,000 cycles per second. This is applied to the wall of the lateral semi-circular canal via a post-auricular incision, with just sufficient removal of bone to allow access. The emitter is applied so that the facial nerve and cochlea are not included in the field of irradiation. Nystagmus is observed to ascertain the various stages in the action of the vestibular system. It is initially directed to the side of the irradiation. When it disappears the dose is increased until nystagmus to the opposite side appears. It was stated that improvement occurred in hearing and that in many cases there was a lessening of tinnitus. The post-operative discomfort with this method is claimed to be much less than after surgical destructive operations. In Arslan's series 95% of his patients lost their vertiginous attacks. The authors then present some details of their six cases.

The Oral Use of Prednisone in Nasal Allergy.

H. J. SHAW AND B. P. SCRIVENER (*J. Laryng.*, October, 1958), discuss the use of prednisone, taken orally, in the treatment of nasal allergy. They state that this method should be reserved for those cases in which treatment by the usual medical and surgical measures has been unsuccessful. They present a series of 28 patients suffering from nasal allergy in whom all other methods had failed, and in whom symptoms and signs were most severe. Prednisone was administered in tablet form. In typical cases the dosage was 5 mg. three times a day for one to two weeks, after which the patients were maintained for a variable period on a minimum dose which would suppress symptoms; in many this was 5 mg. or 2·5 mg. daily. The length of treatment varied between three and 12 weeks. Side effects were mild, being seen in only two patients, one of whom had an erythematous rash on the face, frequency of micturition and some abdominal distension. The other suffered temporarily from nausea. Six of these patients were classified as "failures"; 22 patients obtained worthwhile relief, but the authors state that eventual relapse appears likely in many cases. However, as this method should be used where other methods have failed, the authors conclude that the oral use of prednisone in the severe forms of nasal allergy is useful and justified.

The Use of Masking in Pure Tone Audiometry.

T. SCHOEL (*J. Laryng.* December, 1958), discusses the use and limitations of masking in pure tone audiometry. The purpose of masking is to eliminate the hearing of one ear in order to avoid response from the wrong ear. The masking mechanism in the inner ear and the relation of the masking effect to the frequency distribution and the intensity of the masking signal, are recorded briefly. The masking effect of white noise may be measured in unilaterally deaf patients by registering the shift of the pure tone threshold produced by increasing masking intensities in the same ear. The effect is fairly equal on air conducted and on bone conducted tones. The masking effect only becomes manifest at a definite threshold, which in this study is 10 to 40 decibels S.L. depending upon the frequency of the masked pure tone. The threshold is lowest in the medium frequencies, in which the dynamic capacity of the ear is greatest, while it is higher in low and high frequencies. Above this "masking threshold" the masking effect rises linearly with the intensity of white noise, i.e. for each 10 decibel increase of the masking intensity the threshold value of the masked pure tone increases by 10 decibels. The degree of the acoustic leakage between the two ears is the deciding factor as to when masking will take place and to what extent. In bone conduction the interaural attenuation for practical purposes equals zero, and therefore masking will always be carried out of the best bone conduction during registration of the bone conduction threshold of the opposite ear. In air conduction the better ear will be masked if the difference between the air conduction loss of the weaker ear and the bone conduction loss of the opposite ear is greater than or equals the interaural attenuation (in this investigation 50 to 60 decibels). The thresholds of cross-masking may be determined by sounding increasing intensities of white noise in the deaf ear of patients with unilateral deafness. Figures are given to show at what intensities of white noise masking occurs in an ear with normal hearing. Figures close to these masking intensities, may be applied as routine values for masking of air and bone conduction, even if the bone conduction loss of the best ear is zero (on condition that the stimuli and the test system have the identical physical characteristics as those applied in this investigation). The highest masking intensities permitted usually suffice to obtain satisfactory masking effect. High-grade conduction loss is an exception. At a difference of 60 decibels between air and bone conduction loss ("gap" value of 60 decibels), the masking effect is nil. On application of a non-linear or not measurable masking signal, it is advised to use the masking method suggested by Zwislocki, a brief account of which is given.

Skin Diving.

J. A. FIELDS (*A.M.A. Arch. Otolaryng.*, November, 1958), discusses the medical problems associated with the sport of skin diving. Most of these, while they are not serious, fall within the field of oto-laryngology. Nose bleeding may occur due to capillary rupture in the nose and sinuses. A condition known as "face squeeze" is brought about when the nose, covered by the face mask, is isolated from the remainder of the respiratory passages; when the palate closes the nasopharynx as the depth of descent increases, the air volume within the mask diminishes, and the face is virtually squeezed into the mask. Ear symptoms are the common complaint for which skin divers consult otologists. One type of ear pain may be related to this "face squeeze". Hæmotympanum has been seen as a sequel to the Eustachian tube air lock persisting and is the counterpart of aerotitis seen in aviation. Retraction of the drumhead due to pressure changes on each side of the drum leads to dilatation of vessels and soon to pain. Further increase of pressure leads to rupture of vessels, releasing blood and serous fluid into the middle ear cavity. Ultimately this may lead to rupture of the tympanic membrane. A similar mechanism leads to sinus pain and bleeding. Most tympanic membrane ruptures occur before the second atmosphere of pressure is reached. In descent, the feeling of pressure in the ears is the signal to attempt a Valsalva manoeuvre which if unsuccessful should mean an immediate ascent. Skin divers should be warned of the damage of practising their sport while suffering from acute upper respiratory infections, allergic attacks, etc. If the membrane ruptures acute otitis media almost always supervenes. Wax or other debris in the external auditory meatus is forced into the middle ear cavity. These perforations usually heal with proper treatment. Otitis of severe degree is seen at times as a result of the bites of sea lice in and around the ear. The appearance resembles herpes zoster oticus. The author recommends the use of a cortisone preparation. He states that labyrinthitis with symptoms of earache, vertigo and deafness is another possible complication, and believes that a condition of hydrops can occur, and that damage to the inner ear by intra-vascular bubble formation is also possible.

Audimutism.

R. AMYOT (*Presse méd.*, July 26, 1958), reports three cases of audimutism in siblings, aged respectively 18, 20 and 21 years. The three affected persons are two females and one male. The parents are in good health and normal, except that the father stammers slightly; they are grandchildren of two sisters, so that there is an element of consanguinity. The three patients were subjected to exhaustive clinical and laboratory investigations, and the author concludes on the findings that the condition in these three cases is not retarded development, but rather a definitive arrest in the evolution of function. As far as speech is concerned, they remain at the two-year-old level. The author describes in detail the accompanying abnormalities affecting the patients, and gives the results of the tests that were carried out. She states that audimutism without partial deafness or verbal deafness, of congenital origin and familial incidence, is a clinical entity of obscure physiological basis. It is clearly distinguished from congenital word deafness with alexia and agraphia, and must not be confused with similar phenomena secondary to lesions of the ganglia or to an extreme degree of mental deficiency.

British Medical Association.

NEW SOUTH WALES BRANCH: SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on June 19, 1958, at the Royal Alexandra Hospital for Children, Sydney. The meeting took the form of a series of clinical demonstrations by the members of the honorary medical staff of the hospital.

Congenital Dermal Sinus Tracts.

MR. M. SOFER SCHREIBER showed three patients to illustrate congenital dermal sinus tracts. He said that abnormal closure of the neural tube was a common cause of congenital defect of the nervous system, and when that abnormal closure presented as a meningocele or as a meningomyelocele it was recognized by everyone. Congenital dermal sinus tracts were a much less well-known form of closure defect. That was unfortunate, because if such a tract was not recognized and adequately dealt with surgically before a spreading infection occurred, a healthy child might be suddenly transformed into one with a cerebral abscess, or paralysed legs and sphincters.

The first patient shown by Mr. Sofer Schreiber was a boy, aged two years and nine months, to whom that catastrophe had happened. He had been well until the age of 15 months, when a small inflammatory lump appeared over the lumbo-sacral part of his spine. The lump was a localized, reddened, cystic swelling with a small central sinus, and it was thought to be an infected pilonidal sinus. He developed neck and back stiffness, and a lumbar puncture was performed; pus was obtained, from which *Proteus* was grown. It was thought that an extradural abscess was present, and a lumbar laminectomy was performed. No extradural abscess was found. The child was now paraplegic and incontinent of urine and fæces, and it was evident that the superficial inflammatory swelling represented infection about the skin end of a congenital dermal sinus tract, and that the paraplegia was due to the inward spread of that infection to form an abscess in the spinal cord itself. A myelogram showed a block at the level of the eleventh thoracic vertebra, and a large spinal cord abscess (probably an infected dermoid cyst of the cord) was found and drained. The child remained paraplegic, he had incontinence of urine and fæces, and he still had a discharging sinus in the back.

Mr. Sofer Schreiber said that spinal dermal sinus tracts were located predominantly in the lumbo-sacral region, whereas the much less important congenital pilonidal sinus (which extended no more deeply than the deep fascia) usually occurred nearer to the anus, in the sacro-coccygeal region. Spinal dermal sinus tracts might also occur at higher levels of the spine, in the thoracic and cervical regions. The sinus opened to the surface as a mid-line dimple, usually only one or two millimetres in diameter. Frequently there was pigmentation or port-wine staining of the adjacent skin, and hairs might or might not protrude from the opening. A tract extended inwards from that dimple to terminate in the meninges or in the substance of the spinal cord, or it might expand intraspinally to form a dermoid cyst. Clinically there was often a history of recurrent inflammation about the skin dimple. There might be a history of one or more bouts of unexplained meningitis, or, as in the case demonstrated, of local intraspinal suppuration. The treatment should be complete excision of the entire dermal sinus tract before infection of the meninges or cord took place.

Mr. Sofer Schreiber then showed a boy, aged five years, who had been first examined at the age of nine months, when he had fever, a stiff back, paralysed legs and sphincters and a *Proteus* infection of a lumbo-sacral dermal sinus tract. The tract was dissected out in continuity with an infected dermoid cyst of the spinal cord. Some leg weakness remained, and an ileal bladder had been constructed to cope with his urinary incontinence.

Mr. Sofer Schreiber said that a similar condition might be seen in the head, nearly always in the occipital region. The skin signs were similar to those of the back, but the skin dimple and the port-wine staining might be difficult to see because of the hair. However, there was often a palpable small subcutaneous thickened area at the site of the dimple. If it was not detected and dealt with, meningitis might occur, or a cerebral abscess might develop, or an associated intracranial dermoid cyst might present as a posterior fossa tumour.

Mr. Sofer Schreiber next showed a girl, aged two and a half years, who had been born with a small lump on the back of her head in the mid-line. It was thought to be a prominence of the bone, and no notice was taken of it until she was two years old, when it was noted that the lump intermittently discharged pus. A close examination of the lump after the hair had been cut showed that it was a small cyst with a central punctum, and that there was some port-wine staining of the surrounding skin. The cyst was in the mid-line just above the external occipital protuberance. An X-ray examination of the skull demonstrated a rounded mid-line defect in the occipital bone, about one centimetre in diameter, lying about four centimetres below the level of the scalp cyst. At operation the superficial scalp cyst was found to be a dermoid cyst attached to a dermal sinus tract, which passed through a small hole in the occipital bone just above the transverse sinus. That small hole was not visible in the X-ray film. The tract then became continuous with a large intradural dermoid cyst, which lay superficially to the cerebellum. The bone defect visible in the X-ray film was superficial to the convexity of the cyst, and was in fact completely filled in with membranous tissue.

Mr. Sofer Schreiber said that because of the disastrous and irreparable effects of inflammatory damage on the nervous system, it was essential that those tracts be recognized and dealt with before such damage occurred. An important corollary was that all infants and children with unexplained meningitis, especially if it was due to the *Staphylococcus aureus*, to *Proteus* or to *Bacterium coli*, should have the entire mid-line of the back and scalp carefully examined for sinus openings.

Vomiting as the Only Clinical Sign of Cerebral Tumour.

Mr. Sofer Schreiber then showed a boy, aged four years, who had been normal until the age of nine months, when he had an attack of diarrhœa and vomiting. He continued to vomit several times a day and became constipated. He had been first admitted to hospital at the age of 23 months, when he weighed 20 pounds and presented no abnormal physical signs other than emaciation. He underwent numerous investigations, including an X-ray examination of his skull and an electroencephalographic examination. All gave negative results save a barium meal X-ray examination, which showed an inconstant œsophageal reflux. As he continued to vomit, he was submitted to exploratory laparotomy; at that operation it was considered that his pylorus was thickened, and a Ramstedt's operation and appendicectomy were performed. However, the vomiting continued unabated, and his weight fell to 18 pounds. Numerous further investigations were performed, and also a gastro-jejunostomy was established. Despite that, he still vomited, and in the absence of organic findings a functional cause was strongly suspected. However, sedation and psychotherapy proved unsuccessful—he continued to vomit.

At that stage, at the age of two and a half years and with a weight of 19 pounds, with a story of persistent vomiting for 21 months or two-thirds of his life and with no abnormal physical signs other than emaciation, a diagnostic lumbar puncture was performed. Unfortunately sedation was not employed, traumatic blood was obtained, and the fluid was discarded. A further puncture one week later produced clear fluid with a protein content of 70 milligrammes per 100 millilitres. The significance of that increased protein content was in some doubt because of the recently obtained blood-stained fluid, but it was considered that air studies were justified, and lumbar pneumoencephalography was performed. No air entered the ventricles, and the cerebro-spinal fluid contained 45 milligrammes of protein per 100 millilitres. A ventriculographic examination was performed, and it was found that the ventricles were of normal size and shape, but the aqueduct and fourth ventricle appeared to be slightly more anterior than usual. The ventricular cerebro-spinal fluid was of normal composition, and a further electroencephalogram gave normal results.

It was not thought that the evidence warranted posterior fossa exploration at that stage. However, the vomiting continued, and a second ventriculogram two months later confirmed the diagnosis; the skull sutures were now separated, the lateral and third ventricles were dilated, the aqueduct and fourth ventricles were definitely displaced forwards, and air did not enter the lower portion of the fourth ventricle. A posterior fossa tumour was clearly present, and was demonstrated at the subsequent craniotomy. A large astrocytoma of the medulla oblongata was projecting posteriorly into the cisterna magna and the lower portion of the fourth ventricle. As much of the tumour as

was possible was removed, and he was subsequently given deep X-ray therapy. After that the vomiting ceased, and the patient rapidly gained weight and normality.

Mr. Sofer Schreiber finally showed a boy, aged 10 years, who had commenced vomiting on April 4, 1958. At first he vomited only after breakfast, later after all his meals. When he was examined by Dr. J. Beveridge on April 29, he was dehydrated and had lost weight. However, there were no signs of nervous system disease. An X-ray examination of his skull revealed no abnormality, and an electroencephalogram showed diffuse dysrhythmia. Lumbar puncture was performed by Dr. Beveridge. The pressure of the cerebro-spinal fluid appeared low (50 millimetres of water), and the fluid contained no cells, but had a protein content of 160 milligrammes per 100 millilitres. In the next few days he manifested slight guarding of his neck. As there were no signs of increased intracranial pressure, a pneumoencephalogram was taken; no air entered the ventricles. A ventriculogram was therefore taken, and it was found that the lateral and third ventricles were mildly dilated, that the aqueduct was displaced forwards, and that only the upper portion of the fourth ventricle filled with air. At the subsequent posterior fossa craniotomy, an ependymoma was found growing from the floor of the fourth ventricle.

Mr. Sofer Schreiber said that vomiting was the outstanding and most constant symptom of tumour of the brain in childhood. It occurred with tumours of any type, in any location, and in almost every case. Usually it resulted from increased intracranial pressure. However, especially in tumours of the brain and posterior fossa, it might occur in the absence of, or before, such generalized increase of intracranial pressure had developed, and vomiting might be the earliest, and for many weeks the only, symptom of such an intracranial tumour. Typically the vomiting caused by cerebral tumour tended to occur in the morning shortly after arising and before breakfast, and it was usually associated with, but not followed by, nausea. Whilst that classical type of vomiting was highly suggestive of a cerebral origin, very often the vomiting due to cerebral tumour did not differ from that induced by other causes, and the repeated vomiting and retching might be accompanied by abdominal pain and discomfort. It was not, therefore, surprising that gastro-intestinal disease should be suspected, and that as a result unnecessary appendicectomies or other abdominal operations should be performed, as in the first case. The only safe rule in a case of persistent vomiting without definite other cause and with an absence of physical signs is to examine the skull radiologically for separation of the sutures, and to examine the cerebro-spinal fluid for an increase in the content of cells or protein.

The Treatment of Acute Leukæmia.

DR. D. G. HAMILTON discussed the treatment of leukæmia in children. He said that it was almost always acute. The child presented with a story of a few weeks of pallor and tiredness. Often there had been fever or purpura, and not infrequently limb pains. The purpura might be marked, slight or absent. Lymph glands might be enlarged. The spleen and liver were often enlarged. Sometimes all those signs were absent, and it was the blood count that gave the diagnosis—a blood count that revealed a normocytic anæmia, a high leucocyte count, many of the cells being primitive forms, and a deficiency of mature granulocytes and platelets. But sometimes the peripheral blood was quite normal. If such a child had limb pains, pallor, tiredness and a raised blood sedimentation rate, the confusion with rheumatism was easy. It was then that bone marrow biopsy gave the diagnosis. The marrow was crowded with leukæmic cells, primitive leucocytes. Until a very few years previously, such a diagnosis meant that the child was left with a few weeks or at the most a few months of life—weeks or months of illness, discomfort, debility and unhappiness. However, now that process could be temporarily reversed in almost all such patients, a further year or so of happy, healthy life could be achieved. Dr. Hamilton mentioned a little girl, in whom acute leukæmia had been diagnosed 15 months prior to the meeting. Within three weeks she became well, and had remained so since.

Dr. Hamilton then said that treatment was by means of the corticosteroids, of which prednisone was the most convenient, the purine analogue 6-mercaptopurine and the antifolic drugs, of which "Amethopterin" was the best. The patient was given an initial transfusion if the blood count was low enough. A start was then made with prednisone, 20 to 60 milligrammes per day for a week, the dosage then being gradually reduced over the next three or four weeks. Mercaptopurine was given from the beginning, too, in a dose of one milligramme per pound of body weight per day. If there was much neutropenia at the onset, some prefer to withhold mercaptopurine at first, for one of its toxic effects was agranulocytosis. By the end of this first month great improvement should have taken place. The child would probably be well, the peripheral blood would be normal or nearly so, and even the bone marrow might be normal. A maintenance course of mercaptopurine of one milligramme per pound, up to 50 milligrammes per day, was continued. Dr. Hamilton said that he continued to give prednisone in a dosage of five milligrammes per day as well, and for a period ranging in his experience from five months to almost three years the child remained well. Blood counts must be made weekly at first and at least every three weeks throughout.

Dr. Hamilton went on to say that certain problems might arise. (i) Marked neutropenia may result. That might be a toxic effect of the mercaptopurine or might indicate a relapse of leukæmia, and bone marrow biopsy was the only way to tell which it was. If that showed a toxic depression of the marrow, mercaptopurine therapy must be stopped, temporarily at least, and administration of prednisone increased to therapeutic dosage. (ii) A relapse of leukæmia might occur, shown clinically by the presence of blast cells in the peripheral blood or by the neutropenia referred to earlier. When that happened, if prednisone had not been given in maintenance dosage, it should be introduced in full therapeutic dosage, and if amethopterin was available, it should replace the mercaptopurine, which was now obviously failing to control the disease. (iii) Neurological signs—headache, papilloedema or cranial nerve palsies—might occur. That was usually due to leukæmic infiltration of the brain and meninges. The drugs given did not pass the blood-brain barrier easily, and the disease might progress in the brain while controlled in the rest of the body. The treatment was X-ray therapy to the head, but usually it meant that the end was not far off.

Dr. Hamilton finally said that treatment was not complete without consideration of the human side of the problem. For the child, doctors must aim at getting as long a span of normal, happy life at home as they could. For the parents, they must have sympathetic understanding. They must tell them the truth as kindly as they could, for the parents knew it. Doctors could promise them something like a year of normal life for their child; but they could leave a gleam of hope, for in each year something new might turn up. Everybody needed and deserved hope, most of all parents facing that tragedy. What hope was there at present? The first hope was that in the next year a new and better drug may be developed, for work was proceeding on those lines at a number of centres. The second hope was that the grafting of healthy bone marrow might become a practical possibility. In that procedure the whole of the leukæmic marrow of the patient was destroyed by X-ray therapy, and then a graft of marrow from a healthy donor was introduced. So far that procedure had not gone beyond the stage of animal experiment.

Indications for Electroencephalography in Children.

DR. L. RAIL discussed electroencephalography in children. He said that the EEG could detect local or generalized changes in brain rhythm. The changes resulted from disturbances in metabolism, which could be caused by pressure or by inflammatory or degenerative changes. If the pathological process was sufficient to disturb the metabolism of the neurons, one could expect evidence in the EEG of those events. However, if the process was temporarily or permanently not active, a normal EEG might result in the presence of disease or cerebral atrophy. One could expect changes that indicated the location, the degree of disturbance, and in some cases more specific ætiological information.

Discussing some cerebral conditions, Dr. Rail said that the EEG was most valuable in obtaining information on epilepsy. In suspected cases, one took an EEG to determine the diagnosis (the presence of epileptic patterns, whether the process was localized or generalized, the site of the irritation causing the seizures) and the treatment (the most suitable type of drug—that, of course, depended on clinical correlations as well as on EEG findings—and when to discontinue drug treatment). The examination could be carried out on patients at any age. In suspected focal lesions of the brain the site of the lesion could usually be determined. Cerebral neoplasms were rare in children, but could be localized in 70% to 80% of cases. Cerebellar neoplasms produced normal records in 40% to 50% of cases, and generalized changes in most of the remainder. That served to distinguish that group to some extent. Cerebral abscess always produced gross abnormality. Serial records showed increase of that abnormal activity. Cerebral venous thrombosis or repeated seizures often produced a similar clinical picture, but could

be distinguished by serial records, as improvement usually occurred in a few days. Thus, in focal lesions, the EEG would help to locate the disease and suggest the aetiology (by serial tracings in doubtful cases of acute onset). In inflammatory diseases, such as meningitis and encephalitis, the EEG indicated the degree of cerebral disturbance, the rate of progression and recovery, and the development of complications, such as subdural effusions or focal damage. Dr. Rail stressed the fact that aetiological information was of little value, except when carefully correlated with the clinical findings.

Referring to cerebral injury, Dr. Rail said that once again the record would indicate the location, the degree of disturbance, the rate of recovery, and any complications (subdural hæmatoma, intracerebral hæmorrhage, post-traumatic epilepsy). Records should be taken within 10 days of a head injury, and serial tracings at intervals of two to six weeks, if evidence for medico-legal purposes was required. In mental defect Dr. Rail said that the examination was carried out to give information on the site and extent of brain damage, and the presence of epileptic disturbances of rhythm, which could contribute to the deficiency.

Cerebral atrophy of long standing was frequently inactive electrically, so that in organic mental defect without epilepsy, about 30% to 40% of subjects would have normal records on routine examination. In behaviour disorders, the EEG might reveal evidence of cerebral damage (e.g., temporal lobe lesions), evidence of epilepsy or signs of cortical immaturity.

In summary, Dr. Rail said that the test was indicated if one suspected local or generalized brain disease of any origin. Careful correlation of the tracings with the neurological picture, and a knowledge of the basic physiology, are essential for good results in clinical practice.

Tracheo-Œsophageal Fistula.

Mr. J. Steigrad discussed tracheo-œsophageal fistula. He said that the object of the presentation was to keep tracheo-œsophageal fistula before the medical practitioner who was customarily in attendance on the newborn baby. To provide every opportunity for surgical relief to be made available, the diagnosis should be arrived at within a period of 24 to 48 hours. Suspicion of the presence of atresia of the œsophagus and a tracheo-œsophageal fistula was aroused when a neonate exhibited excessive salivation and episodes of cyanosis, particularly following attempts at feeding. A size number 10 Jacques catheter was passed into the œsophagus, and if it would not go beyond a distance of approximately 12 centimetres measured from the upper alveolus, presumption of the presence of œsophageal atresia was implied. An amount of about one or two cubic centimetres of "Lipiodol" was injected through the catheter, and X-ray pictures were taken with screen control. The opaque medium was then sucked out.

Mr. Steigrad then described the case of a female infant, third in the family, 36 hours old. The mother had had hydramnios. The child's birth weight was five pounds two ounces, and she had salivated a lot since birth. Coughing and cyanosis followed attempts at feeding her. The diagnosis was suspected at the base hospital, and X-ray pictures were taken. The infant was sent to the Royal Alexandra Hospital for Children and operated on when 48 hours old. The anomaly discussed was revealed, the fistula was closed, and an anastomosis was made between the proximal and distal ends of the œsophagus. The infant was sent home to the country, cured, after one month.

Mr. Steigrad then gave the clinical history of another child, a male, 48 hours old. There was no history of hydramnios. He had had much mucus from birth, and returned all feedings with much mucus and cyanosis. An X-ray examination revealed a tracheo-œsophageal fistula. Operation was performed, and the result was adequate except for some stenosis at the site of anastomosis. Repeated œsophageal dilatations were performed by Mr. N. Meacle, and progress had been satisfactory.

Mr. Steigrad said that the condition was not uncommon. Since 1953, 40 cases had been dealt with at the Royal Alexandra Hospital for Children. The over-all recovery rate of 10% was poor, but the results over the past 12 months had been better than in the previous years. In summary, the following points were important: (i) The condition was not uncommon. (ii) Suspicion should be aroused if a newborn infant had excessive salivation and episodes of cyanosis. (iii) A history of hydramnios in the mother was suggestive. (iv) The diagnosis could be arrived at at any centre with adequate X-ray equipment. (v) Operative treatment should be undertaken at a centre equipped with surgical, senior resident and nursing staff trained in the care of babies with that congenital abnormality.

Coarctation of the Aorta.

Mr. Douglas Cohen presented a male child, aged three years, with coarctation of the aorta. Operation in March, 1958, had shown the coarctation to be at the classical level; a patent ductus arteriosus and marked post-stenotic dilatation were also present. The coarctation did not appear to allow any blood at all to pass. A resection and end-to-end anastomosis were performed successfully.

Mr. Cohen said that 10 patients, aged from four to ten years, had been operated on in the last two years without mortality. One child, aged three months, had died suddenly in hospital prior to operation. The series did not include 16 patients with so-called "infantile coarctation", eight of whom had been submitted to operation. That condition bore no real relation to true "adult coarctation", and had been designated "the hypoplastic aortic arch syndrome"; it was the subject of a separate communication at present awaiting publication.

Mr. Cohen went on to say that in his unit the term "coarctation" was reserved for cases in which there was a narrowing of the aorta—usually extreme—distal to the subclavian artery. The ductus, which was patent in about 20% of those cases, opened just proximally to the site of narrowing. The precise anatomy varied considerably from case to case. The children usually presented with an undiagnosed systolic murmur. On further examination, the femoral pulses would be found to be absent or markedly diminished when compared with the radial pulses. If the peripheral pulses were checked in all cases in which a systolic murmur was found to be present, many more cases of coarctation would be diagnosed in childhood. Moreover, operative correction could be undertaken with greater safety, since it was much easier in childhood. The time of election was approximately eight years, by which time the diameter of the aorta was adequate to prevent any recurrence of the stenosis, even if the suture line failed to grow at the same rate as the aorta. However, if any degree of hypertension was present, operation should usually be advised earlier. When the condition was diagnosed in infancy, the usual mode of presentation was either as failure to thrive or as congestive cardiac failure. In such cases, after a preliminary period of medical resuscitation, operation should usually be undertaken. Even when no symptoms were present, operation should always be advised when the child was about eight years old, provided that the diagnosis had been made early enough. The mortality was low, and without operation the patients usually died in the third or fourth decade from a variety of causes associated with their lesion, whereas there was good reason to believe that a successful resection of the coarctation should restore a reasonably normal life expectancy in all cases.

Chronic Urinary Tract Infection.

Dr. John McDonald said that chronic urinary tract infection in childhood was a relatively common condition, and often posed many problems in diagnosis and management. The difficulties encountered in controlling and eradicating infection in chronic and recurrent pyelonephritis were many, in general being related to two main groups of patients. First, there were those children with a chronic infection associated with the presence of an anatomical abnormality of the urinary tract, which was often not able to be corrected surgically. Secondly, there were those without any obvious anatomical abnormality, in whom treatment of the urinary infection was often complicated by the emergence of drug-resistant organisms, or by superadded infection with a different organism. The diagnosis of a chronic urinary tract infection is frequently overlooked, because patients with such infections might complain of no symptoms for long periods of time. Furthermore, an appreciable number of patients with chronic pyelonephritis might show on occasions little or no pyuria in the presence of bacilluria and a culture of microorganisms for the urine, so that unless a full bacteriological as well as microscopic examination of the urine was carried out, an accurate diagnosis might not be reached. The first two cases illustrated those points well.

Dr. McDonald then showed a girl, aged four years, who had a history of recurrent dysuria, frequency of micturition and bed-wetting of three months' duration. Treatment of her recurrent urinary infections had consisted of several short courses of a sulphonamide and chloramphenicol. Each period of treatment had been followed by temporary relief of her symptoms and normal urinary findings, but a relapse occurred soon after treatment was stopped. On her admis-

sion to the children's hospital she was found on repeated occasions to have no pyuria, but *Bacterium coli* in heavy growth was recovered persistently from her urine. As the organism was sensitive to tetracycline and streptomycin, treatment was started with the former drug, but after eleven days the urine still yielded *B. coli* on culture, although pyuria was again absent. As the organism had now developed resistance to tetracycline *in vitro*, the treatment was changed to a prolonged course of streptomycin and nitrofurantoin, with rapid disappearance of organisms from the urine. Full radiological and cystoscopic examination failed to reveal any structural abnormality of the urinary tract. The child subsequently had continued to be symptom-free, and her urine had remained free of pus cells and sterile on culture. Dr. McDonald said that the patient demonstrated the fact that pyuria (arbitrarily defined as five or more leucocytes per high-power field in a centrifuged specimen of five millilitres of urine) was at no time present in the specimens of urine examined, while undoubted urinary tract infection was present. Furthermore, the development of drug resistance was a factor in the initial failure to eradicate her infection.

The second patient shown was a girl, aged 10 years, who had been first examined after a week's history of frequency and scalding on micturition and bed-wetting. Examination of a catheter specimen of urine revealed four to six leucocytes per high-power field, and a culture produced a heavy growth of *B. coli*. She was treated for three weeks with a sulphonamide, after which further examinations of four successive catheter specimens of urine showed the persistent presence of *Streptococcus fæcalis* on smears and in cultures, although pyuria was absent on all occasions. The child was free of symptoms during that time. Treatment with an appropriate antibiotic, tetracycline, was then continued for six weeks, during which period the results of further urine examinations remained normal. Three days after the treatment ceased, the girl again complained of frequency of micturition and bed-wetting, and on further examination of the urine numerous pus cells were found for the first time, many Gram-negative bacilli were seen in smears, and a heavy growth of Proteus resulted from culture. Appropriate chemotherapy was again instituted, with rapid clearing of her urine. Dr. McDonald said that the girl was now symptom-free, and no abnormality was detected on radiological examination of the urinary tract. Repeated microscopic and bacteriological examinations of her urine had continued to give normal results. She was continuing to take small daily doses of sulphafurazole for a prolonged period. The outstanding feature of her case was the absence of pyuria, except on two occasions, while at the same time organisms were seen in smears of the urine and grew on culture. Furthermore, three different organisms had been recovered on successive cultures of the urine, each of which was without doubt indicative of a true urinary infection. In addition, the second episode of infection was completely devoid of any symptoms related to the urinary tract.

Dr. McDonald's third patient was a girl, aged three years. He said that although she had been treated for frequent urinary tract infections over the preceding nine months, her long history of recurrent fevers suggested that those infections had been present for two years previously. Her urine had been found to be loaded with pus on many occasions, and those recurrent *B. coli* infections had prompted many unsuccessful investigations to ascertain the existence of some anatomical abnormality of the urinary tract. Intravenous and retrograde pyelography along with cystoscopic examination had failed to reveal any underlying urinary tract anomaly responsible for the recurrent infections. The clue to the diagnosis was the finding of a persistently positive response to the double micturition test—the child was able to pass an appreciable amount of urine two minutes after an initial micturition. In the absence of an abnormal urinary stream and of evidence suggesting an abnormality of the bladder or urethra, a positive response to the double micturition test suggested the diagnosis of congenital megaureter with ureteral reflux. That condition, which was far from rare in childhood, could often be diagnosed conclusively only by means of a cystourethrogram taken during micturition. A congenital left megaureter with free reflux was in fact demonstrated in that patient by means of that technique. The constant urinary stasis which was present in such patients was responsible for the development of infection in the urinary tract. The cystourethrogram taken during micturition demonstrated the gross reflux of dye up the left megaureter particularly during micturition, the normal urethral shadow and the complete emptying of the bladder at the very end of micturition. However, an X-ray film taken two minutes after the completion of micturition revealed the fact that the ureter had emptied all the dye back into the bladder again. Such was the basis of the diagnostic double micturition test and the therapeutic triple micturition procedure which, performed twice daily, was usually sufficient to keep the bladder free of residual urine and thus help obviate infection. The prolonged use of an appropriate antibacterial agent in conjunction with that procedure is necessary to overcome existing infection and to help keep the urinary tract free of further infections.

Childhood Schizophrenia.

DR. MARJORIE GILCHRIST showed two children with schizophrenia, a girl, aged five years, and a boy, aged ten years, who had been attending the child guidance clinic at the hospital since October, 1957. Both children had shown extreme restlessness from about the age of two years, and there was a lack of normal speech development. When first examined at the clinic, they were so withdrawn that they made practically no contact with people. Their speech consisted of irrelevant responses to questions, or the repetition of phrases used in conversation to them at home. Their mental ages, so far as could be estimated by appropriate tests, were well below their chronological ages.

Dr. Gilchrist said that the object of discussing the children was to emphasize the importance of a correct diagnosis and the need for early treatment. Schizophrenic children were frequently diagnosed as defective children, and were not given the intensive treatment needed to counteract their withdrawal. The five-year-old girl had been able to commence schooling at a normal school, and had improved considerably. The ten-year-old boy had improved to a limited extent only, and attended the Education Department's class at a school for mentally handicapped children.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

ANNUAL REPORT OF THE PRINCE ALFRED HOSPITAL, SYDNEY.[1]

[From the *Australasian Medical Gazette*, March, 1895.]

THE annual report of the P.A. Hospital, Sydney, for 1894 shows that during the past year 2927 patients have been treated, as against 2611 in 1893. Of these 175 were inmates of the hospital on December 31, 1893, and of the 2752 admitted during the year, 787 were cases of accident or urgency, 1043 were received under Government vouchers, and 901 contributed more or less to the cost of their maintenance. The mean residence of the patients had been 27 days as against 29 in 1893, and the rate of mortality had been 9·74 against 9·92. The attendance of outdoor and casualty cases had been 35,136 against 31,258 in 1893.

Correspondence.

INFLUENZA ON A VESSEL TRAVELLING TO AUSTRALIA.

SIR: It is thought that there may be some interest by your readers in an outbreak of influenza which occurred recently on a mail boat travelling from the United Kingdom to Australia.

The R.M.S. *Himalaya*, carrying 704 first-class passengers, 398 tourist passengers and a crew of 638, left Tilbury on February 12, 1959, and arrived at Fremantle on March 6, via Port Said, Aden and Colombo. There had been an epidemic of influenza in London before the ship sailed, and during the voyage 167 cases were reported, the first case within a few hours of leaving Tilbury. Within three days of leaving Tilbury, 40 cases had medical attention, and the peak was reached shortly after leaving Suez on February 19, 1959, and the last case occurred six days prior to arrival at Fremantle. At Aden the quarantine authorities refused permission for passengers to go ashore.

[1] From the original in the Mitchell Library, Sydney.

Clinically, the patients showed remarkably constant symptoms and signs, with an incubation period of about three days. All ages were affected, except that no cases were seen in babies under six months. A few of the Asian crew were affected, and their symptoms were the same as those of the Europeans. Onset was sudden, with general aches and pains chiefly in the muscles. Average peak temperatures were between 100° and 101° F., with a maximum of 102° F. Over half the cases had a non-productive cough. Every case seen showed without exception an œdematous pharynx. Duration of the illness was about 72 hours.

Recovery was complete in all cases, but two cases had complications. A female of 27 developed lobar pneumonia, which quickly responded to treatment, and a male, aged 72, developed a post-influenzal depression, which also responded to treatment. Treatment in all cases was symptomatic.

Yours, etc.,

A. J. Metcalfe,
Director-General of Health.

Commonwealth Department of Health,
Canberra, A.C.T.,
March 18, 1959.

THE BILLY GRAHAM CRUSADE IN SYDNEY.

Sir: During the Dr. Billy Graham Crusade at the Sydney Showground from April 12, special arrangements have been made through the Christian Medical Fellowship for doctors and their families. A reserved area has been set aside under shelter in the members' stand, in which a telephone has been installed. The phone number is 35-9141. Should a call be received, the usher in attendance will page the doctor concerned in the reserved area.

Due to the large crowds expected, reserved seats will only be held until 7.15 p.m., after which they will be open to the general public.

To obtain tickets, doctors may ring WM 3786 from Monday to Friday, and the tickets will be posted to them. There is no charge for any seat.

Yours, etc.,

Douglas Trehoar,
Chairman, Christian Medical Fellowship.

135 Macquarie Street,
Sydney,
March 23, 1959.

CORTISONE AND CORNEAL ULCERATION.

Sir: Is it possible to warn, or perhaps advise, practitioners of the extreme danger to sight of using cortisone preparations in the eye in corneal ulceration? Should this ulceration be due to the herpes febrilis virus, then a large spreading, and indeed blinding, keratitis is the result.

These ulcers, especially in children, may show as a slightly pink eye with some irritation. One or two days of cortisone therapy as drops will, indeed, in many instances, cause a large ulcer covering half the cornea to be present, and the probability of greatly reduced vision. This effect is widely known amongst ophthalmologists; but distressingly many instances of the use of cortisone in red eyes are apparent.

In the interests of the prevention of some loss of sight usually and much suffering, could this be propagated amongst all our members?

Yours, etc.,

John L. Bignell.

2 Collins Street,
Melbourne,
Victoria.
March 24, 1959.

GROWING UP IN A CHANGING WORLD.

Sir: In recent issues of the Journal there have been discussions anent the behaviour of youth, capped by your leading article in the March 7 issue. It seems strange that none of the speakers or writers seem to have taken into account the basis of human society, viz., the relations of production.

The relations of production undeniably determine the sphere, the objective and the methods of attaining the latter for the youth.

There are on the globe today two kinds of human society—capitalism and socialism—with profoundly different relations of production. In the former, juvenile delinquency is universally increasing; in the latter it has decreased and become almost negligible. A socialist economy is based on the collective ownership of the means of production, and means therefore a planned economy whose objective is to bend nature to man's needs. This ensures that an extraordinary variety of occupations becomes available to all the youth. They therefore can develop their talents and exercise them in a sphere suitable to them.

Education, as is well known, is provided for all at no personal cost. A tremendous healthy, sane social opinion is formed, so everything in socialism combines to give youth an active, busy, intellectual and physical life, devoted at once to their individual interests and to those of all their fellows.

It is therefore obvious why delinquency has waned. I trust that some of your readers will tell us to what percentage of our youth present capitalism and its crises are providing praiseworthy objectives and the means to achieve them.

Yours, etc.,

G. P. O'Day.

196 Nepean Road,
Aspendale,
Victoria.
March 12, 1959.

The Royal Australasian College of Physicians.

SCIENTIFIC MEETING AT PRINCE HENRY'S HOSPITAL, MELBOURNE.

The Victorian Fellows and Members of The Royal Australasian College of Physicians will hold a scientific meeting at Prince Henry's Hospital, St. Kilda Road, Melbourne, on Saturday, May 2, 1959. The programme is as follows: 11.30 a.m., "The Venous Pulse", Dr. K. Fairley; 12 noon, "Lipid Metabolism and Arterial Disease", Dr. J. Bornstein; 1.45 p.m., "Surgery of Arterial Disease", Mr. K. N. Morris; 2.15 p.m., "Use of Diuretics", Dr. M. V. Clarke; 2.45 p.m., "The Role of Phonocardiography in the Assessment of Systolic Murmurs", Dr. J. M. Gardiner; 3.45 p.m., "Management of Cardiac Pain", Dr. Allan Wynn. All members of the medical profession are invited to attend this meeting.

The College of General Practitioners.

QUEENSLAND FACULTY.

Queensland Centenary Post-Graduate Week-End.

The Queensland Faculty of the Australian College of General Practitioners is holding its Queensland Centenary Post-Graduate Week-end at Surfers' Paradise, Gold Coast, from May 1 to 4, 1959.

The programme is as follows:

Friday, May 1, at 8 p.m.: Reception and registration at the Chevron Hotel, Surfers' Paradise.

Saturday, May 2, Paradise Room of the Surfers' Paradise Hotel: 9.30 a.m., opening of the week-end by the Honorable the Minister for Health and Home Affairs, Dr. H. W. Noble; 10 a.m., "Placental Insufficiency", Dr. Lionel P. Sapsford; "Ophthalmic Difficulties", Dr. Daniel Hart; 11.30 a.m., "The Diagnosis of Pigmented Skin Tumours", Professor Maurice Ewing, Professor of Surgery, University of Melbourne, guest lecturer; 2 p.m., panel discussion, "Arteriosclerosis, its Genesis and Management", moderator, Dr. Kurt Aaron; panel members, Dr. Harry G. Wilson, Dr. Redmond L. Quinn, Dr. Graham H. Neilson; 3.45 p.m., "Diagnosis and Treatment of Common Skin Diseases", Dr. Lorna M. Archibald. 8 p.m., informal fork dinner at the Southport Golf Club.

Sunday, May 3, Paradise Room of the Surfers' Paradise Hotel: 9.30 a.m., "The Present Status of Treatment of Tuberculosis", Dr. Ellis W. Abrahams; "How Can the G.P. Assist in the Problem of the Aged?", Dr. Alan Knyvett; 11.30 a.m., "The Management of the Lump in the Breast", Professor Maurice Ewing; 2 p.m., "The Significance and Management of Cardiac Arrhythmias", Dr. Harry G. Wilson; "How Can the Pathological Laboratory Help the G.P.?", Dr. Redmond L. Quinn; 3.45 p.m., "The Diagnosis and Treatment of Swellings in the Inguinal Region in Children", Dr. Peter Grant; "The Prevention of Post-Partum Hæmorrhage", Dr. Lionel P. Sapsford.

The week-end course is open to all medical practitioners, whether they are general practitioners, specialists, members of the College or otherwise. A special invitation is extended to interstate visitors. Accommodation is available at the Chevron Hotel, Surfers' Paradise, but members may stay elsewhere on the Gold Coast if they so desire. If accommodation is required, it will be arranged by the Secretary on request. The fee for the course and social activities is £7 7s., to cover a medical practitioner and the person accompanying him or her. All who propose to attend are asked to advise the Honorary Secretary, Box 1498V, G.P.O., Brisbane.

The College of Radiologists of Australasia.

EXAMINATION RESULTS.

THE following candidates were successful in the March, 1959, examinations of The College of Radiologists of Australasia, Part II, for membership of the College:

Radiodiagnosis: Dr. A. J. T. Aram, Dr. E. N. Kurrle, Dr. A. F. L. Neal (Victoria); Dr. J. F. Ryan, Dr. W. R. Cautin (New South Wales); Dr. R. M. Chrisp, Dr. R. D. Gibson (New Zealand).

Radiotherapy: Dr. G. F. Adler, Dr. P. R. Leckie (Victoria).

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Annual Subscription Course.

DR. ORVAR SWENSON, Clinical Professor of Pædiatric Surgery, Tufts University School of Medicine, and Surgeon-in-Chief, Boston Floating Hospital for Infants and Children, will give the following lectures in the Main Lecture Theatre, Royal Alexandra Hospital for Children, as part of the annual subscription course: Monday, April 13, at 8 p.m., "The Diagnosis and Treatment of Congenital Aganglionic Megacolon with Particular Reference to Long-Term Results"; Wednesday, April 15, at 8 p.m., "The Cord Bladder in Children".

SEMINARS AT SYDNEY HOSPITAL, MAY AND JUNE, 1959.

THE following seminars at Sydney Hospital will be held in the Maitland Lecture Hall on Wednesdays, from 2 to 3 p.m. Each seminar will be preceded by medical grand rounds at 12 noon (Maitland Lecture Hall), lunch in the Board Room and a pathological demonstration in the Maitland Lecture Hall at 1.30 p.m.

May 6, "Diabetic Problems", Dr. F. Hales Wilson (Royal North Shore Hospital); May 13, "Acute Medical Conditions of the Chest", Dr. J. G. Richards (by invitation), thoracic clinic; May 20, "Newer Viruses", Professor P. M. de Burgh (Department of Bacteriology, University of Sydney); May

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MARCH 7, 1959.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2	1(1)	1(1)	..	1	..	..	..	5
Amœbiasis	..	..	..	1(1)	..	..	..	..	1
Ancylostomiasis	..	..	1	..	..	..	6	..	7
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	1	..	..	..	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	3(3)	10(8)	10	..	..	..	1	..	24
Diphtheria	1(1)	..	..	..	..	..	..	..	1
Dysentery (Bacillary)	..	3(3)	3(1)	3(3)	3	..	..	..	12
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	74(38)	16(13)	12(6)	27(5)	..	..	3	..	132
Lead Poisoning	..	..	1(1)	..	..	..	..	..	1
Leprosy	..	1(1)	..	..	..	..	2	..	3
Leptospirosis	1	..	3	..	..	..	..	..	4
Malaria	..	1	1	..	..	..	..	..	2
Meningococcal Infection	1	1	..	..	..	..	..	..	2
Ophthalmia	..	..	..	..	8	..	..	..	8
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	..	..	..	..	..	..	..	..
Puerperal Fever	1	..	2	..	..	..	..	..	3
Rubella	..	21(18)	..	1(1)	6(5)	1(1)	..	..	29
Salmonella Infection	..	..	..	1(1)	1(1)	..	..	..	2
Scarlet Fever	12(5)	16(11)	8(7)	..	1(1)	1(1)	..	..	38
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	1	1	..	..	..	..	2
Trachoma	..	..	..	..	..	..	39	..	39
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	23(17)	5(4)	16	6(5)	6(3)	1	..	..	57
Typhoid Fever	..	..	..	..	1	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

27, no seminar—The Royal Australasian College of Physicians' meeting; June 3, "Hysteria", Dr. A. T. Edwards, psychiatry clinic; June 10, "The Types of Hypertension that may be Relieved by Treatment of the Primary Lesion', Professor R. Farquharson (University of Toronto); June 17, "Radiology of the Upper Gastro-Intestinal Tract", Dr. H. B. L. Williams, gastro-enterology clinic; June 24, "The Endocrine Management of Disseminated Carcinomatosis", Dr. K. S. Harrison (by invitation), Mr. E. Wilson, Dr. P. F. Hall, endocrine clinic.

All medical practitioners are invited to attend these seminars.

Notes and News.

Third Australasian Conference on Radiation Biology.

An organizing committee is arranging, in association with the Radiation Society, the third Australasian Conference on Radiation Biology, to be held at the University of Sydney from August 15 to 18, 1960.

It is expected that two or more guest speakers will deliver addresses to the conference on the primary biochemical and biological lesions in radiobiology, chemical and biological protection and the delayed somatic effects of radiation.

Papers, in general of 2500 words (250 word summary), are invited in radiation biology, radiation chemistry and radiation physics. Accommodation will be available at the University of Sydney. Further announcements will be made. The Convenor is Dr. Peter Ilbery, Department of Preventive Medicine, University of Sydney, Sydney, N.S.W.

The Australian College of General Practitioners: Victoria Faculty.

On March 19, 1959, the Victoria Faculty of the Australian College of General Practitioners inaugurated what it hopes will become a permanent feature of post-graduate education in Victoria. A series of medical films were shown in the theatrette of Imperial Chemical Industries of Australia and New Zealand, I Nicholson Street, East Melbourne. More than 60 doctors, members and associates of the Australian College of General Practitioners and members of the British Medical Association, attended. It is intended that films drawn from the libraries of ethical drug houses and the Melbourne Medical Post-Graduate Committee, films made by specialists in Melbourne and other cities, and films from the libraries of trade commissioners of other countries, will be regularly shown on the third Wednesday of each month at the theatrette. All members of the British Medical Association are invited to attend. The Faculty is indebted to I.C.I.A.N.Z., Melbourne, for courteously making available the theatrette for this purpose, and for the provision of supper after the showing of the films.

The New South Wales Sports Medicine Association.

A meeting of the New South Wales Sports Medicine Association will be held at 8 p.m. on April 15, 1959, in the Council Room of the National Fitness Building, Macquarie Street, Sydney. Mr. Forbes-Carlile will read a paper entitled "The Electrocardiogram of the Fatigued Athlete". All those interested are invited to be present.

Medical Appointments.

Dr. O. E. J. Murphy has been appointed a member of the Queensland State Committee of the Commonwealth Scientific and Industrial Research Organization.

Nominations and Elections.

The undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Bridger, Allan Joseph, M.B., B.S., 1956 (Univ. Sydney), 5 Sargood Street, O'Connor, A.C.T.

Hatos, George, M.D., 1937 (Univ. Szeged) (registered in accordance with the provisions of Section 17 (1) (b) of the *Medical Practitioners Act*, 1938-1958), 29 Canter Street, Cammeray.

Johnston, Colin Ivor, M.B., B.S., 1958 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Phillips, John Keith Andrew, M.B., B.S., 1957 (Univ. Sydney), 84 Cook Road, Centennial Park.

Stepan, Jaroumira Frances, M.D., 1946 (Univ. Prague) (licensed in accordance with the provision of Section 21 (*b*) of the *Medical Practitioners Act*, 1938-1958), Mental Hospital, Stockton.

Diary for the Month.

April 13.—Victorian Branch, B.M.A.: Finance Subcommittee.
April 14.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
April 15.—Western Australian Branch, B.M.A.: General Meeting.
April 16.—Victorian Branch, B.M.A.: Executive of Branch Council.
April 18.—Victorian Branch, B.M.A.: Country Branch Meeting (Warrnambool).
April 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

Medical practitioners are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales. Anti-Tuberculosis Association of New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

All articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given, surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to The Medical Journal of Australia alone, unless the contrary is stated.

All communications should be addressed to the Editor, The Medical Journal of Australia, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

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